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SALMONELLA DUBLIN MENINGITIS

REPORT OF A CASE COMPLICATED BY A RIGHT SUBDURAL EFFUSION

H. L. UTIAN, M.B., B.C.H. (RAND.)

The Fever Hospital, Johannesburg

Though generally speaking not a common condition, *Salmonella* meningitis occurs not infrequently in infants, and should always be borne in mind in the diagnosis of a purulent meningitis in a patient of this age-group. The literature has been extensively reviewed, first by Henderson¹ in 1948 who collected 144 cases, to which he added 3 cases of his own, and later in 1951 by Beene, Hansen and Fulton,² who reported 87 further cases, one of which was their own. The series collected by Henderson, who was able to report on the use of sulphonamides and penicillin, had an over-all mortality of 86%. Beene *et al.*, making the comment that despite the use of other antibiotics such as streptomycin and chloramphenicol, their mortality was not much better, reported an 82% mortality. Since this time sporadic reports have been appearing of infants with *Salmonella* meningitis of one type or another who have recovered on antibiotic therapy, the youngest being 19 days old. The following is an account of a 3-months-old infant with *Salmonella* meningitis who developed a right-sided subdural effusion but recovered. It is the first case of *Salmonella* meningitis known to occur at the Johannesburg Fever Hospital.

CASE HISTORY

P.H., aged 3 months, was admitted to the Fever Hospital, Johannesburg on 28 September, 1956 with a 3-day history of fever and a cough, associated with mild constipation. On the morning of admission he had had two fits, each lasting about 5 minutes, in which he had gone blue and stiff, with his head and eyes deviating to the right.

His mother stated that her pregnancy and labour had been quite normal, the birth weight of the baby being 6 lb. 4 oz. He had been cyanosed at birth and had been kept in oxygen for the first week of his life.

Since this time he had been quite well apart from the fact that on a couple of occasions he had been noticed to go blue and stiff, the whole episode lasting a few seconds only. Weight gain had been satisfactory on a dried-milk mixture, and on admission he weighed 10 lb. 12 oz.

On the day of admission the baby was severely ill, with a rectal

temperature of 105°F. He was having almost continuous fits, in which his head and eyes deviated to the right. The neck and back were very stiff and the anterior fontanelle was bulging. The skull circumference was 14½ inches. His throat was mildly inflamed, with slight tonsillar enlargement, and the right ear-drum showed some reddening. Breath sounds on the right side of the chest were harsh and there were scattered rhonchi in both lung fields. The abdomen was soft and not distended, the liver being palpable about 1 inch below the costal margin as a firm, smooth, non-tender mass. The hamstrings were markedly tight, the reflexes brisk and equal and the plantar responses flexor, and there was no apparent muscular weakness.

Lumbar puncture was performed. The cerebrospinal fluid showed on direct examination about 500 polymorphs per c. mm., and no bacteria were observed on a Gram's stain. The total protein was 40 mg. per 100 ml., sugar 49 mg. per 100 ml. and chlorides 123 mEq. per litre. The haemoglobin was 10·1 g.%, the red-cell count 3·6 millions per c. mm. and the leucocyte count 3,600 per c. mm. (47% neutrophils, 51·5% lymphocytes and 1·5% monocytes).

The child was thought to be suffering from a purulent meningitis, and was put on penicillin, 250,000 units 6-hourly, and streptomycin, 0·25 g. twice daily, both by injection, his fits being controlled with phenobarbitone. The fluid intake was quite adequate and intravenous therapy was therefore not considered necessary. He remained very ill for 2 days and then began to improve subjectively, though the temperature remained constantly high between 103° and 104°F. Three days after admission (on 1 October), the South African Institute for Medical Research isolated a *Salmonella*, at first from the CSF, but later from the blood as well. This was identified 2 days later as *Salmonella dublin*, being two-plus sensitive *in vitro* to penicillin, chloramphenicol, chlortetracycline, oxytetracycline, tetracycline and neomycin, but not to streptomycin. On 1 October therefore, the regime was changed to chloramycetin palmitate 100 mg. 4-hourly and penicillin 250,000 units 6-hourly.

The temperature still remained high, and 5 days after admission the patient again had a few mild fits lasting a few seconds only, in which he became mildly cyanosed, with his head and eyes turned to the right. The lumbar puncture was repeated and the fits controlled by increasing the phenobarbitone. The CSF, on this occasion contained 43 polymorphs and 25 lymphocytes per c. mm., total protein 52 mg. per 100 ml., sugar 23 mg. per 100 ml. and chlorides 123 mEq. per litre. *S. dublin* was isolated from the fluid, this time being three-plus sensitive to streptomycin and chloramphenicol. Streptomycin was again given and the child began to improve, his temperature reaching a normal level after 10 days in hospital. Cerebrospinal fluid and blood were

still positive on culture for *S. dublin* on 5 October. The Widal test at this time had been negative on 2 occasions. On 9 October the haemoglobin was 9.1 g.%, leucocytes 12,700 per c. mm. (54% neutrophils, 42.5% lymphocytes, 2.5% monocytes, and 1% eosinophils). Blood culture was still positive at this time. Physical signs remained very much the same, except that the patient now developed a right external-rectus palsy and was thought to be slightly deaf.

The child in himself gradually began to look much better, though his temperature again began to rise slightly. He became progressively more deaf and his sight, too, began to deteriorate. His weight had remained more or less static, and after 2 weeks in hospital he weighed 10 lb. 14 oz. In view of the persistently positive cultures, the antibiotics were persisted with until 19 October, when he had been in hospital for 3 weeks. On this date the cerebrospinal fluid contained 5 polymorphs and 6 lymphocytes per c. mm., total protein 14 mg. per 100 ml., sugar 43 mg. per 100 ml. and chlorides 120 mEq. per litre. The haemoglobin was 11.5 g.%, and the white cells 13,700 per mm. (51.5% neutrophils, 44.5% lymphocytes, 2.5% eosinophils, 1.5% monocytes and 0.5% basophils). The Widal on 13 October gave a positive 1 : 200 titre to *S. typhi O*, and on 19 October a positive 1 : 4,000. Both cerebrospinal fluid and blood were now completely sterile.

All treatment was therefore stopped at this juncture. The child now began to look very well. The temperature was normal and sight and hearing rapidly began to return to normal, though the right external-rectus palsy remained. The weight after 4 weeks in hospital was 11 lb. 5 oz., and this gain continued until his discharge over 5 weeks later, when he weighed 14 lb. despite his further setbacks.

The temperature remained normal for a week after the cessation of therapy, when it again began to rise, though the baby appeared to be quite well. Chloramphenicol was started again on 25 October, and on 26 October lumbar puncture and subdural taps were performed. No fluid was obtained on the left side, but on the right side about 5 c.c. of a thick, straw-coloured fluid was aspirated, which clotted on being left to stand. This fluid contained 14 polymorphs, 52 lymphocytes and 1,000 red cells per c.mm., the total protein more than 500 mg. per 100 ml. and chlorides 122 mEq. per litre. *Salmonella dublin* was isolated from this. The cerebrospinal fluid taken at the same time contained 7 polymorphs and 21 lymphocytes per c.mm., total protein 18 mg. per 100 ml., sugar 53 mg. per 100 ml. and chlorides 123 mEq. per litre. This was sterile. Following this procedure, he ran a temperature of 102.6°F and became fairly ill. This settled down after 72 hours on penicillin and his cover of chloromycetin, the temperature remaining normal for the remainder of his stay in hospital.



Fig. 1. Lateral view of skull showing size of the effusion.

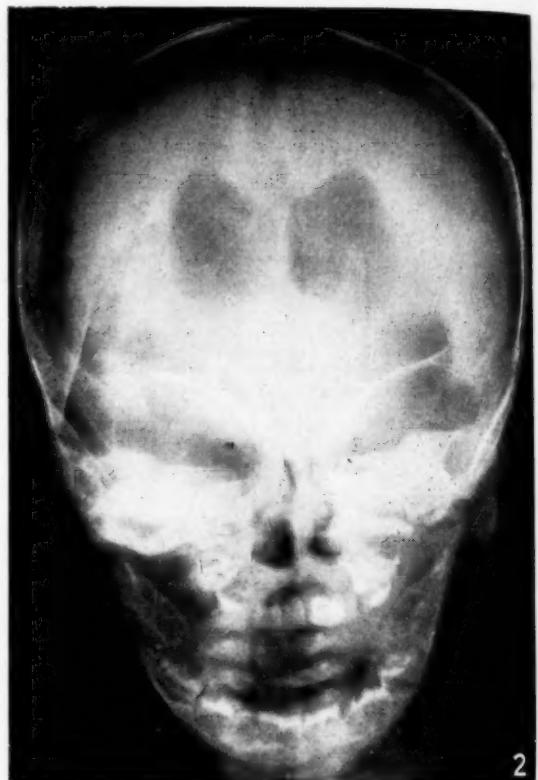


Fig. 2. P.A. view of skull showing air in the ventricles and in the right subdural space.

On 30 October, 4½ weeks after admission, he appeared quite well. Mental development appeared to be quite normal for his age, and he was quite normal on physical examination except for his squint. The skull circumference was 14½ inches—a gain of ½ inch in one month. Blood culture was sterile. The Widal gave *S. typhi O* agglutination up to 1 : 200, haemoglobin was 12.5 g.%, and the leucocyte count was normal with a normal distribution.

Five weeks after admission, on 2 November, the subdural taps were repeated, together with a lumbar puncture. On this occasion 8 c.c. of a thick yellow fluid was aspirated on the right side. This fluid contained 1 polymorph, 4 lymphocytes and 1,045 red cells per c.mm. with a protein of 240 mg. per 100 ml. and a sugar of 33 mg. per 100 ml. Both CSF and subdural fluid were sterile on culture. The following day 8 c.c. of fluid were withdrawn from the subdural space and 50 mg. of streptomycin were injected.

The taps were not repeated until 11 days later. The skull circumference was now 15½ inches—an increase of 1 inch in 2 weeks. The right side of the head appeared to be expanding more than the left, with the right frontal eminence protruding in front of the left. On this occasion 5 c.c. of a thick yellow fluid was obtained, with a protein of more than 500 mg. per 100 ml. The CSF was quite normal and was sterile, as was the subdural fluid. A week later the fluid had definitely increased and 12 c.c. of a thin yellow fluid was obtained with ease, again with a protein of over 500 mg. per 100 ml. On 23 November, 2 days later, and 7½ weeks after admission, an air encephalogram was performed and air was put into the subdural effusion. This showed a fair degree of dilatation of the ventricular system, suggesting the presence of an external hydrocephalus and a huge subdural effusion over the whole of the right frontal area (see X-rays in

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Figs. 1 and 2). On 26 November 1956, therefore, the patient was transferred to the Princess Nursing Home, Johannesburg, for removal of this effusion.

On 28 November Mr. E. R. Rosenberg operated. A right frontal flap was raised, a subdural membrane being found over the right frontal area as far back as the motor cortex. The outer membrane was stripped from the dura, but the inner membrane had to be left because it was attached to the pia and attempts to remove it caused bleeding. There was also a fairly severe arachnoiditis.

After this operation the child made an uninterrupted recovery except for a few mild fits involving the left side of the body, which were controlled with phenobarbitone. Shortly before discharge he had a mild temperature which subsided on chloromycetin. The skull circumference remained at 15½ inches until discharge on 21 December 1956, 12 weeks after admission. He appeared to be fairly normal mentally and is to be followed up for the possible development of hydrocephalus.

DISCUSSION

Henderson mentions that of all *Salmonella* infections—*S. enteritidis*, *S. dublin* and *S. choleraesuis* appear to have the strongest predilection for the meninges. He quotes Bornstein as dividing the *Salmonellae* (excluding *S. typhi*) into 3 clinical groups, viz.

1. Those causing gastro-enteritis with vomiting, diarrhoea and mild fever.
2. Those causing a fever milder than typhoid, and lasting 1-3 weeks.
3. Those causing septicaemia with a high remittent fever, positive blood-culture, and localization which may occur anywhere in the body.

The severity of the illness therefore appears to depend on the type of organism, its virulence and its affinity for a particular tissue. The other factor, at any rate for *Salmonella* meningitis, appears to be the age of the patient. Of Henderson's cases, 60% occurred before the age of 3 months, a further 12% between the ages of 3 and 6 months, 10% from the age of 6 months to 2 years, 9% from 2 to 15 years and 9% in the remaining years of life. From this series, therefore, it would appear that the maximum incidence of *Salmonella* meningitis occurs before the age of 3 months, and that thereafter the incidence drops sharply, 3/4ths of the cases of *Salmonella* meningitis occurring before the age of 2 years. This would appear to be due to the fact that the meningitis in children up to the age of about 3 months are an area of *locus minoris resistentiae*—to *Salmonella* infections in particular. Other factors that predispose to the development of *Salmonella* meningitis are the presence of other meningeal infections, such as meningococcal and syphilic meningitis.¹

Salmonella infections are notorious for the manner in which they present, and this is especially the case in children,² in whom an atypical presentation is almost the rule. This case bears this fact out, for it was pulmonary and central-nervous-system symptoms that brought it to hospital. Of 7 cases of *Salmonella* meningitis reported at various times in the literature since 1950³⁻⁶ only 3 had gastro-intestinal symptoms as part of their disease.

Therapy is complicated, and chloramphenicol does not appear to be as specific for the *Salmonella* infections as was first thought. The antibiotics and chemotherapeutic agents used in the treatment of the abovementioned 7 infants, who recovered were chloramphenicol in all 7 cases, penicillin in

7, streptomycin in 5, chlortetracycline in 4, oxytetracycline in 1, sulphadiazine in 4 and gantrisin in 1. The practice at present followed would thus appear to be to use 2, 3 or even 4 antibiotics or chemotherapeutic agents at one time. This is perhaps understandable, but it would be as well to remember that antibiotics are not necessarily synergistic, and may in fact be antagonistic.

The development of subdural effusions after purulent meningitis is not at all an uncommon event, and is always worth watching for as a cause of unexplained pyrexia or central-nervous-system symptoms.^{4, 5} This was exemplified in the case here reported, for while he was developing his effusion, his only sign of ill-health was the presence of a persistent temperature. However, Henderson mentions only one of his cases as having had an effusion, and of the recent cases, only that of Beene *et al.*, had a possible collection of fluid in the subdural space. This anomaly may be explained by the fact that until the introduction of sulphonamides very few cases of *Salmonella* meningitis lived long enough to develop effusions that could be detected clinically. Of 50 cases of subdural effusion complicating bacterial meningitis in infants and children described by McKay, Ingraham and Matson⁶ in 1953, most occurred after influenzal meningitis, but they also mention pneumococcal and meningococcal meningitis as causes of effusion. Another important point mentioned by these authors is that of 47 cases of bacterial meningitis under the age of 1 year treated by them in 3 years, 60% developed subdural effusions—truly a complication that must be watched for.

The therapy of *Salmonella* meningitis has advanced a long way in the last 25 years, but the problem of treatment has certainly not been solved, and there is a very urgent need for an antibiotic that is completely efficacious in this disease.

SUMMARY

A case of *Salmonella* meningitis complicated by the development of a right-sided subdural effusion from which the organism was cultured is described.

A brief summary is made of the age incidence, presentation therapy and complication by subdural effusion of *Salmonella* meningitis.

I would like to thank Dr. A. L. Jackson for permission to publish this report and also for his help, advice and criticism in its preparation. My thanks also go to Dr. Scott-Miller, M.O.H. of Johannesburg for his permission to publish this, to Mr. Rosenberg for his permission to publish an extract of his notes on the operation, and the Photographic Unit of the Witwatersrand University, Department of Medicine for photographing the X-rays.

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VAN DIE REDAKSIE

IONISERENDE BESTRALING

Gedurende die jongste tyd het daar 'n aantal artikels in mediese tydskrifte verskyn oor die gevare verbonde aan blootstelling aan X-strale en gamma-strale.^{1,2} Die hoeveelhede van die gevaarlike strale wat gedurende gewone radiologiese ondersoeke aanwesig is en op die pasiënte gerig word, is ondersoek en vasgestel, en die gevare, asook die minimale gevaarlike dosisse, kan tans akkuraat bereken word. Behalwe die welbekende nadelige uitwerkings van bestraling wat lank reeds bekend is en waarop die strengste publieke gesondheidsreglemente van toepassing is, blyk dit dat daar 'n ander minder-bekende gevaar is wat as gevolg van die uitspreidings-effek van selfs baie klein dosisse op die hals gehaal kan word; hierdie uitwerkings is die ernstigste wanneer hulle geneties is, en om genetiese uitwerkings te veroorsaak, is dit waarskynlik nie nodig dat die testikels of eierstokke direk bestraal moet word nie. Dit blyk dat selfs baie geringe mate van bestraling die chromosome onder sekere omstandighede onherroeplik kan beskadig. Afgesien dus van die onmiddellike plaaslike uitwerkings op die bestraalde liggaamsdeel, word diepgaande uitwerkings oor die liggaam aangetoon, en veral die voortplantingselle word geskaad.

As gevolgtrekking, wat onlangs van 'n statistiese ontleding gemaak is,³ is verstaan dat ongeveer 10-15 kinders elke jaar weens leukemie in Engeland sterf, waarskynlik as gevolg van 'n enkele blootstelling aan 'n diagnostiese skiaogram kort voor geboorte. 'n Totaal van 1,500 gevallen van kinders onder die ouderdom van 10 jaar is gevind en, in 'n sorgvuldig-beheerde toets het hierdie navorsers 'n skynbaar belangrike toename in die sterftetal weens leukemie en ander kwaadaardige gewasse by kinders, wie se moeders aan bekkenmeting en ander X-straal diagnostiese metodes gedurende die betrokke swangerskap onderwerp was, gedemonstreer. Geen soortgelyke toename van sterfgevalle is tot dusver by kinders, wat pas na geboorte bestraal is, aangeteken nie. Of voorgeboortelike blootstelling 'n etiologiese faktor is, sal in die toekoms volledig bespreek en ondersoek word deur radioloë dwarsdeur die wêreld. Daar bestaan heelwat twyfel oor die statistiese geldigheid, maar dit is goed bekend dat fetale weefsels besonder gevoelig is vir bestraling. Bekkenmeting vereis 'n dosis bestraling wat oor die hele liggaam aangewend word, en op die onbeskermde fetale weefsels gerig word.⁴ Hierdie bevinding het 'n hele reeks artikels as gevolg gehad waarin die gevare, wat tot dusver as onskadelike radiodiagnostiese metodes beskou was, onder bespreking gekom het.

Daar radiodiagnostiese masjiene vervaardig word wat

EDITORIAL

IONIZING IRRADIATION

There has recently been appearing in the medical literature a number of publications on the dangers of exposure to X-rays and gamma-rays.^{1,2} The quantities of the dangerous rays present and directed onto the patients during ordinary radiological examinations have come under investigation and have been determined, and the hazards as well as the minimal dangerous doses are coming to be accurately assessed. It appears that, in addition to the well-known ill-effects of irradiation, which have been recognized for many years and for which public-health regulations of the most stringent kind are in force, there is another less well-known risk which may be incurred as a result of the scatter effect of even very small doses; these effects are most serious when they are genetic, and to produce genetic effects it is apparently not necessary that the testes or ovaries should themselves be directly irradiated. It appears that even very small irradiation may do irreparable harm to the chromosomes under certain circumstances. Apart, therefore, from the immediate local effects in the area irradiated, profound effects are registered on the whole body and they are most profound on the reproductive cells.

As a conclusion recently drawn from a statistical analysis³ it has been stated that about 10-15 children die in England every year from leukaemia which has probably been induced by the single exposure to a diagnostic skiagram shortly before birth. A total of 1,500 cases of children under the age of 10 years have been found and 'these workers, in a carefully controlled experiment, have demonstrated an apparently significant increase in the number of deaths from leukaemia and other malignant tumours in children whose mothers had been subjected to pelvimetry and other X-ray diagnostic procedures during the relevant pregnancy. No similar increase in deaths has thus far been recorded in children X-rayed postnatally. Whether prenatal exposure is an aetiiological factor will be fully discussed and investigated by radiologists throughout the world in the years to come. At present the statistical validity is very much open to question, but it is well known that foetal tissues are particularly sensitive to radiation. Pelvimetry involves a dose of whole-body irradiation directed towards the unshielded foetal tissues'. These findings have set off a whole train of articles

envoudig is om te gebruik, en soos hulle goedkoper word en makliker aangeskaf kan word, kan al hoe meer lede van die professie bekostig om hulle te koop en vir diagnose te gebruik. Dit mag nodig wees om 'n einde te maak aan die onverantwoordelike gebruik van hierdie masjiene en jouself af te vra: „Is hierdie X-straal regtig nodig?“ Dit is duidelik dat ons nie hier met 'n skadelose of onskuldige netode te doen het nie; die spookgestalte het gedaante aangeneem en ons moet sorg dat hy behoorlik ingekerker word.

Wetgewing mag binnekort in sommige lande ingedien word om die onverantwoordelike gebruik van X-straal diagnostiese masjiene te beperk. Die eerste stap gaan ooglopend wees om die gebruik daarvan deur diesulkes wat hoëgenaamd geen geneeskundige kwalifikasies het nie, te verban; onder andere sal sodanige wetgewing die gebruik van hierdie X-straalmasjiene vir die pas van skoene, wat so'n uitstaande kenmerk van ons groter skoenwinkels geword het, verbied. Voordat X-straalmasjiene beskikbaar was, het skoemakers reeds skoene met sukses laat pas, en in elk geval kan die sagte dele van die voet nie onder die fluoroskoop gesien word nie.

As ons onself leer om eers te wag en te dink elke keer voordat ons 'n X-straal neem of voordat ons 'n pasiënt aan fluoroskopie onderwerp, bestaan daar geen twyfel dat die totale hoeveelheid van bestraling aansienlik sal verminder nie. Hierdie vrywillige inkorting van die hoeveelheid bestraling is misken die beste wyse om die probleem die hoof te bied. Indien wette ingestel word om radiodiagnose te beperk, laat hulle gerig wees teen soutiewe masjiene en masjiene wat so saamgestel is dat die filtreerders deur ongemagtige en dwase werkers verwijder kan word. Laat die stral vir sodanige onverantwoordelike gepeuterter verhoog word en laat daar opgetree word teen hierdie onverantwoordelike persone.

Ten laaste sal 'n ernstige navorsingspoging stellig ingestel word om die gevoeligheid van die versterkingskermes en van X-straalfilms te verhoog; hierin het ons misken die maklikste en mees aanneembare metode om die hewigheid van blootstelling te verminder.

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3. Stewart, A. et al. (1956): Lancet, **2**, 447.

in which the risks of what have hitherto been considered innocuous radiodiagnostic manoeuvres have come under consideration.

As radiodiagnostic machines are made which are simpler to use, and as they become cheaper and more readily available, more and more members of the profession can afford to buy and use them for diagnosis. It may be necessary to call a halt to the indiscriminate use of these machines and to ask oneself the question 'Is this X-ray really necessary?' It is manifest that we are not dealing with a harmless and innocuous agent; the genie is out of the bottle and we must be careful to see that his chains are fairly and squarely in place.

Legislation may shortly be introduced in some countries to restrict the indiscriminate use of X-ray diagnostic machines. The first step is obviously going to be to ban their use by such people as have no medical qualifications at all; among other effects the legislation will forbid the use of those X-ray machines for fitting shoes which have become so prominent a feature in our larger shoe stores. Shoes were successfully fitted by shoemakers for many years before X-rays machines were available, and in any case the soft parts of the foot do not show up under the fluoroscope.

If we train ourselves to stop and think every time we have to take an X-ray or before we subject a patient to fluoroscopy, there is no doubt that a considerable reduction in the total quantity of exposure will be achieved. This voluntary reduction in the amount of irradiation is perhaps the best way to face the issue. If laws restricting radiodiagnosis have to be made, let them be directed against faulty machines and machines which are so constructed that their filters can be removed by unauthorized or unwise operators. Let the penalties for such irresponsible tinkering be increased and let action be taken against these irresponsible persons.

Finally there is bound to be a strong development of research for increasing the sensitivity of the intensifying screens and of X-ray films; in this way we have perhaps the easiest and most acceptable method of reducing intensity of exposure.

1. Durbach, D. (1957): S. Afr. Med. J., **31**, 187.
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INTERPROFESSIONAL CIVILITIES

Members of the medical professional are well aware that a medical practitioner may be called upon to defend his action before the Medical Council if he casts reflection upon the probity or professional reputation or skill of a fellow practitioner. Not every doctor, however, realizes that he exposes himself to the same danger if he makes a defamatory statement concerning a registered chemist and druggist, nurse, midwife, auxiliary (physiotherapist, radiographer, etc.), or medical or dental student. This is in virtue of Ethical Rule No. 15 made under the Medical, Dental and Pharmacy Act 1928 by the South African Medical and Dental Council, which includes the following in the list of acts or omissions that constitute conduct of which the Council may take cognizance for disciplinary purposes:

'Unjustifiably casting reflection by word or implication upon the probity or professional reputation and skill of a fellow practitioner, or any other person registered under the Act, or the Nursing Act, 1944.'

This matter came before the last annual general meeting of the Pharmaceutical Society of South Africa, when the attention of the meeting was called to the fact that a similar prohibition is applied to chemists and druggist by the rules of the South African Pharmacy Board. Registered nurses and midwives are subject to a similar prohibition by the rules of the South African Nursing Council.

It is unnecessary to stress the importance of compliance with these rules.

POLYVINYL SPONGE FOR AORTIC GRAFTS

ROBERT H. GOETZ, M.B., CH.B. (CAPE TOWN), M.D. (BERNE), M.D. (FRANKFURT)

Vascular Investigation Service, Groote Schuur Hospital, Cape Town, and Department of Surgical Research, University of Cape Town

Although aneurysms of the abdominal aorta have always been known to have a prognosis as bad as many types of cancer, the diagnosis remained, until very recently, of academic interest only, because curative treatment was unknown and attempts at palliation with few exceptions, had not given encouraging results. This holds good for partial or complete ligation, for wrapping procedures in an attempt to strengthen the wall, and for wiring which aimed at the same effect by promoting partial thrombosis. Resection of the aneurysm with restoration of the defect by means of a graft seemed the only procedure which could result in a cure. The serious prognosis was sufficient justification for considering a more definite approach to the treatment in the hope of lengthening the short life expectancy.

The last few years have brought a complete change in the outlook for patients suffering from aortic aneurysms. Since the initial successful experiments with grafting in cases of coarctation some 5 years ago (Swan *et al.*,¹⁹ Gross *et al.*,²⁰), excision of the aneurysm and bridging of the defect by an interpolated graft is gradually being accepted as the treatment of choice.⁴ Although autogenous material would have been most desirable, the original work was carried out with arterial homografts since no expendable blood vessel was available for bridging a defect in so large a vessel in man. To be used on a larger scale, however, homografts have many disadvantages, such as

- (1) difficulty of supply,
- (2) difficulty arising from storage and sterilization, and
- (3) the fact that disproportions are common because grafts obtained from normal persons have usually to be fitted into patients with grossly diseased vessels.

Homologous grafts do not survive and are replaced by tissue from the host. The graft serves merely as scaffolding for the invading cells. There appeared, therefore, no reason for insisting on viability and most methods of preserving arterial grafts in use to-day, such as freeze-drying, make no effort to keep the tissue viable.

As a logical development of this experience, the possibility of using a non-biological inert material to replace the homologous human graft has been given serious consideration. After numerous efforts with intubation of arteries and replacement by rigid or semi-rigid tubes, Voorhees, Jaretski and Blakemore,²¹ in 1952, succeeded in replacing segments of the aorta in dogs with pliable grafts made of Vinyon-N cloth, throwing the field wide open to experimental work in the search for a suitable material.

The advantages of a readily available tailor-made graft of non-biological origin are apparent. Owen¹⁵ and Scales¹⁷ have listed the properties of the ideal material for a vascular prosthesis. There are additional ones which we should like to include, making it indeed a formidable list:

1. High tensile strength in the wet state.
2. No loss of strength after being implanted in the body.
3. Resistant to hydrolysis and chemical action. Seamless and smooth inner lining.
4. Non-thrombogenic.

5. Great flexibility without kinking. No signs of fatigue.
6. Elasticity permitting pulsation in harmony with the vessels between which it is interpolated.
7. Porous outer surface to permit fibroblasts to anchor the graft in the body.
8. Ease of manufacture.
9. Ease of suturing.
10. Should not wrinkle.
11. Easy to sterilize.
12. Non-carcinogenic.
13. Absence of allergy or sensitization.

The ideal substance has not yet been found, but a large number of cloths woven of plastics such as Orlon, Nylon, Teflon, Saran and many others have now been tried by various groups of surgeons.^{5,7,13,14,16}

Failures with plastic prostheses made from cloth can all be related to unavoidable wrinkling of various degrees,^{1,8,20} the direct result of the non-yielding inelastic character of the material. This renders accuracy of insertion a critical factor.²⁰ Other causes of failure have been related to disproportion between the graft and the recipient aorta.⁶

A relative newcomer in the field which may help to overcome some of these difficulties is Polyvinyl sponge, which was first introduced into medicine by Grindley and Clagett¹ and was originally used for other than arterial work.^{9,10} We have been using Polyvinyl sponge for the last 3 years, first in animals and more recently in human work.

Polyvinyl sponge is a white, light-weight, wettable and resilient material, the cut surface resembling a slice of white bread. It is manufactured from polyvinyl alcohol and formaldehyde by a commercial process and is available in blocks under the names of Ivalon or Prosthex. The blocks are easily sliced on a bacon-slicer for moulding into various shapes. Ivalon is not affected by weak or strong alkali, weak or moderately strong acids and it may be sterilized in boiling water. After cooling, Ivalon keeps the form which has been imposed on it during boiling. Tubes of different sizes can thus be fashioned before or during an operation by wrapping Ivalon round moulds of various diameters. This is important as it will probably never be possible to get a sufficiently large variety of grafts made of plastic cloth by a commercial manufacturer. However, the graft so fashioned loses its shape if it is sterilized once it is taken off the mould.

Ivalon has many advantages over other non-biological materials:

1. It does not produce folds or wrinkles.
2. It handles, feels and sutures like a normal artery.
3. The prosthesis does not collapse but remains open.
4. It kinks less than cloth.
5. The wall of the Ivalon prosthesis is porous, but does not sift blood.
6. The prosthesis is readily incorporated into the neighbouring tissue. It is invaded by fibroblasts after the spaces have been filled by fluid and fibrin. Ivalon has not the

tendency to foreign matter.

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Fig. 1. Bi

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tendency to become encapsulated which occurs with other foreign materials.

However, the most important difference between grafts made of Ivalon and grafts made from other materials—and one which has not been fully appreciated—is that Ivalon is not only pliable but elastic. Thus the graft dilates with each systole like, and in harmony with, the normal artery. This is in sharp contrast to other materials which, although pliable, once incorporated in the body act like rigid tubes and not like elastic arteries. In fact Ivalon grafts behave so much like the normal arteries that if they are fitted in a stretched state they may be used to partially bridge creases.

Being elastic, Ivalon grafts react and respond to stresses and strains in the same way as the normal arterial wall. This is not only of academic interest, but of great practical importance. An Ivalon graft which had been obtained 11 months after it had been inserted was perfectly patent and had been very well incorporated. However, on inspection it exhibited a dilatation just distal to the proximal suture line. When the specimen was opened along its length it became obvious there was a stenosis of the proximal suture line, and the dilatation was of the nature of a post-stenotic aneurysm such as is seen in normal arteries under similar circumstances. This is of great interest since the aneurysm developed in a non-biological material. If the graft had been a rigid tube a stenosing suture could not have produced the post-stenotic dilatation.

It is from this most desirable property, that complications arise. Indeed, there have been more failures with Ivalon⁵ grafts than with any other prosthesis.^{3,5} Weakening, aneurysms and rupture through the prosthesis have been reported by numerous authors.^{1,2,5,7} In fact Deterling and Bhonslay⁷ have reported 100% rupture of this prosthesis when used for the thoracic aorta. This, in our opinion, is of particular significance since the arterial wall at this site has to fulfil the important function of a *Windkessel*.

From our experience in dogs it would appear that aneurysm formation and rupture of a straight graft are either due to disproportion between the vessels of the host and the graft or to stenosis at the proximal suture line. In the Y-shaped graft a further consideration enters the picture, namely a disproportion between the terminal aorta and the iliac vessels, which has hitherto not been sufficiently considered

as a cause of serious complications. Thus the construction of the graft becomes of prime importance.

Various methods of making grafts have been recommended, but no-one seems ever to have given special consideration to the relative diameters of aorta and iliac arteries. If the material is non-yielding and inelastic, this is of no consequence provided the material is strong enough to withstand the internal pressure. However, if the material is elastic the internal diameters become of importance and in order to obtain satisfactory function the physical properties of the prosthesis must closely approximate to that of the artery which it replaces.

On theoretical grounds the blood flow through both iliacs should approximate to that through the terminal aorta:^{*}

$$\text{blood flow } \underset{\text{aorta}}{\sim} 2 \times \underset{\text{iliac}}{\text{blood flow}}$$

According to Poiseuille's Law the flow varies with the fourth power of the radius. Conditions of flow are the same for both the terminal aorta and the common iliacs so that we can re-write our formula:

$$\underset{\text{aorta}}{r^4} \sim 2 \times \underset{\text{iliac}}{r^4}$$

From this formula it is obvious that the radius of the iliac arteries must be considerably larger than is commonly assumed. In fact with an internal radius of 6 mm. of the terminal aorta, the radius of the iliacs should approximate to 5 mm. in order to secure a proper 'run off' in these vessels.

In order to test the validity of this concept, the diameter of the vessels were measured in aortograms obtained in patients not suffering from vascular diseases. As Fig. 1 demonstrates the diameters of the terminal aorta and the iliac vessels are indeed of such dimensions as to support our concept. We, therefore, have constructed our moulds for Ivalon grafts following these principles, i.e. the radius of the various limbs are of the dimensions demanded by the equation. In 7 patients suffering from aortic aneurysms these grafts were inserted and in none has any weakening or aneurysm formation been observed. It was interesting

* As the 2 lowest lumbar arteries come off just above the bifurcation, the blood flow through the terminal aorta is somewhat larger than that through both iliacs.

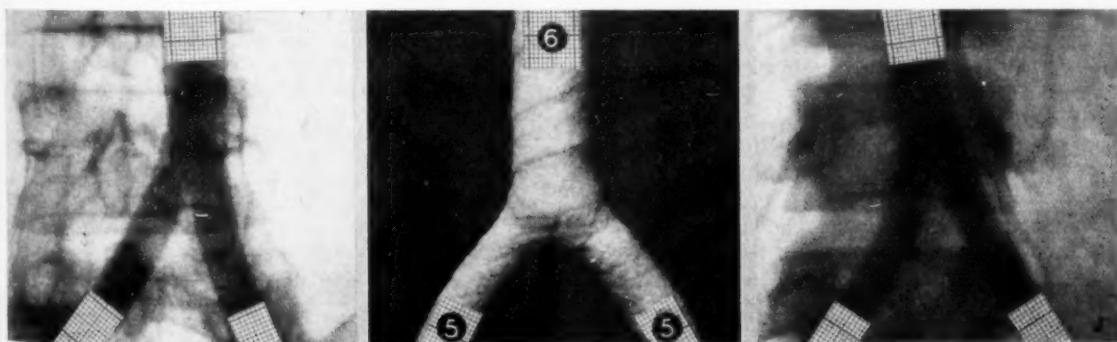


Fig. 1. Bifurcation of the aorta in 2 cases with normal vessels to illustrate the relation between diameter of the terminal aorta and common iliac arteries. An Ivalon graft is shown with similar internal diameters, i.e. a radius of 6 mm. in the aorta and of 5 mm. in the iliac arteries.

to see in all of them how the graft was pulsating in harmony with the vessels into which it had been interpolated.

(We have had the opportunity of measuring the mould used by a colleague who had experienced aneurysm formation. We could demonstrate that the radius of the iliac vessels was only about one-half that of the terminal aorta. Everything else being equal, the "run off" through the two iliac vessels of such a graft is only one-eighth of the flow through the terminal aorta, which in our opinion is sufficient to account for the development of an aneurysmal dilatation and rupture through the graft.)

MANUFACTURE OF THE GRAFT

A. The Mould.

The general design is readily apparent from Fig. 2. There is nothing special about the design except that the diameters are determined by applying the formula set out above.

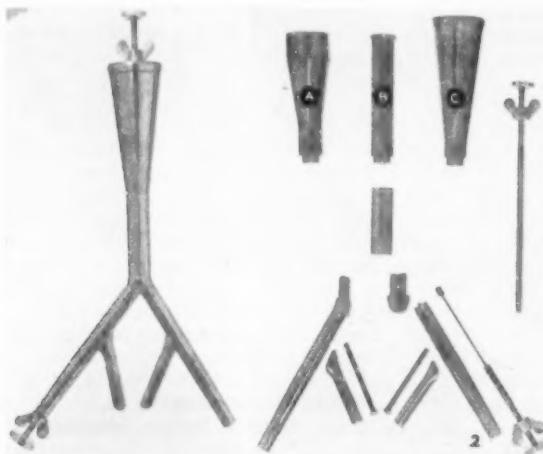


Fig. 2. One of the moulds used for constructing Y-shaped prostheses to replace the bifurcation of the aorta. Radius of terminal aorta, 9 mm. Radius of iliac artery, 7 mm. The mould can be taken apart, as shown, so as to prevent damage to the inner lining of the graft on its removal. The internal iliac is only fitted in exceptional cases.

A number of sizes of moulds have been made, the diameter of the aorta varying by 1 mm. The diameter of the iliac arteries varied accordingly. Special cones can be attached for cases in which the proximal end has to be sutured to an aneurysmal dilatation of the aorta.

B. Principle of Preparing the Graft

This differs in some points from that published by other authors.¹⁸ In covering the mould with Ivalon great care is taken that the thickness of the graft is even throughout. The dry Ivalon bricks are cut with a bacon slicer into sheets 3 mm. thick. One of the sheets is now cut to form a cross of such dimensions that when it is folded over the mould it will comfortably cover all limbs (Fig. 3, A and B). This is sutured into place on either side to form a perfectly even first layer of the Y-shaped graft. It is carefully inspected to assure that the metal of the mould is completely covered (Fig. 3 C). If there are any larger holes in the Ivalon sponge

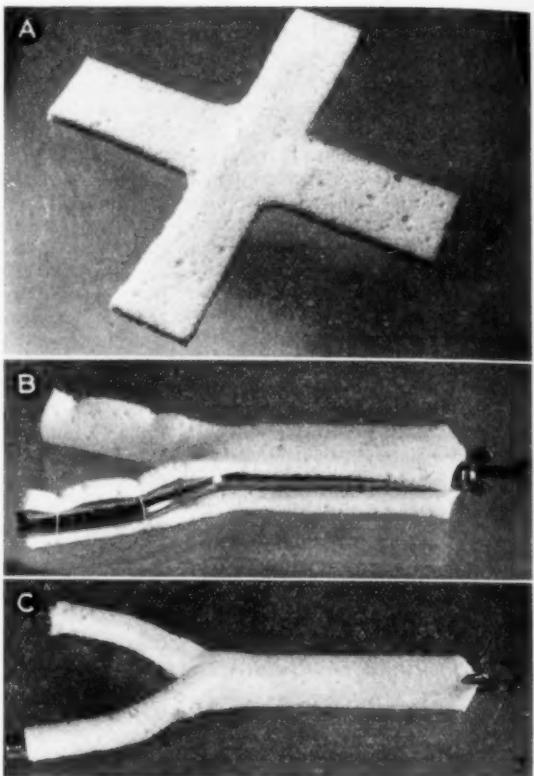


Fig. 3. The first step in the manufacture of the Y-shaped Ivalon graft. The sheet is cut to form a cross, folded over the mould and sutured into place. Note the perfectly even cover obtained.

a piece of Ivalon is fixed in place, if necessary by a single stitch. After this inner layer of Ivalon a single layer of Nylon net is wrapped round the mould. It is kept in place by a few interrupted sutures. Next, a second layer of Ivalon is applied in exactly the same way as the first, and in such a manner that the suture lines are as much out of register as possible. Lastly a strip of Ivalon is wrapped round the aortic limb so that the turns do not overlap, providing one more layer of Ivalon. Thereafter a bandage is wrapped as tightly as possible around the entire mould. It is important that the bandage shall compress the Ivalon sponge evenly and shall not produce strictures. Mould and material are now boiled in water for 15-30 minutes to effect sterilization, and to unite the strips into a single layer (Fig. 4). The Nylon net is firmly incorporated like an internal elastic membrane, for the Ivalon unites through the openings, which would not be possible if cloth were used. The graft is removed from the mould under sterile conditions and kept in sterile saline until sutured in position. It will not keep its shape if re-sterilized after removal from the mould. The inner surface is smooth and glistening, similar to that of the intima, and the outer aspect is rough and affords a firm anchorage for the surrounding tissue.

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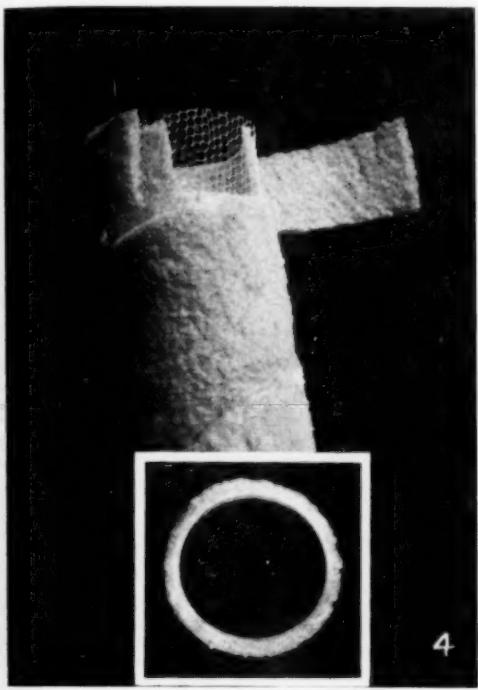


Fig. 4. Aortic end of the Ivalon graft and transverse section. Note the even thickness, the smooth inner surface. The outer layer of the Ivalon has been dissected and reflected and a piece of the inner layer removed to show the Nylon net incorporated between layers of Ivalon.

RESULTS

Ivalon grafts are readily accepted by the tissues of the host. Being pervious they successfully promote arteriogenesis. Fig. 5 illustrates a graft which was removed from a dog 11 months after it had been implanted. At the time of removal it was functioning perfectly well and showed no

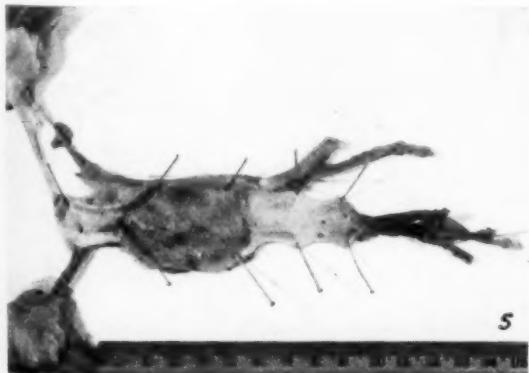


Fig. 5. Ivalon graft in aorta of dog sacrificed almost 1 year after insertion. No signs of thrombosis. Scale shows inches.

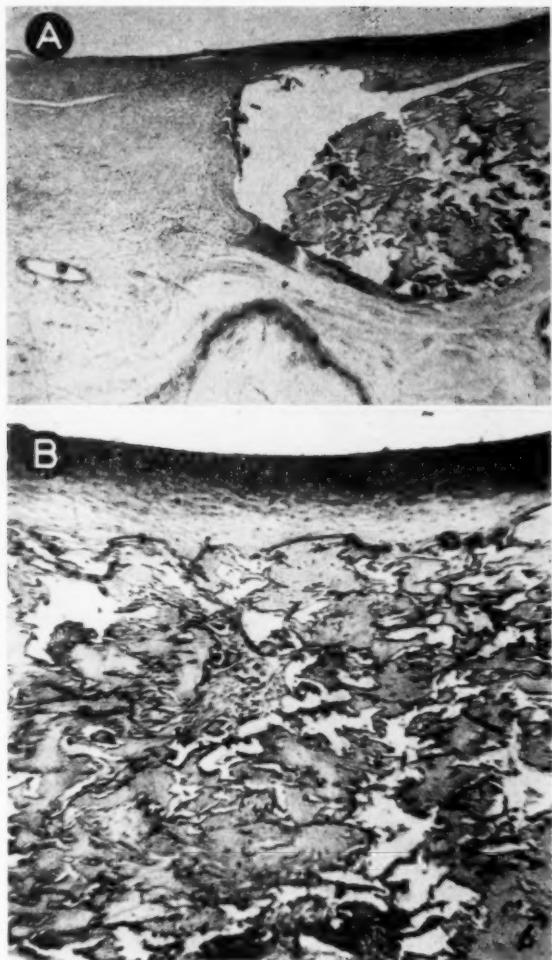


Fig. 6. A. Longitudinal section across suture line between aorta and Ivalon graft. Note the smooth cover of the suture line and the continuation of the intima from aorta to graft. Dog 11 months.

B. High power to show incorporation of Ivalon. Note pegs of fibrous tissue in interstices of graft.

signs of thrombosing. The histological sections showed the inner layer of the plastic to be lined by a smooth layer of organized fibrin deposit with flattened cells resembling true endothelium. This is continuous with the vessel of the host above and below the graft, smoothly bridging the suture line and forming a permanent functional layer (Fig. 6A). This layer was relatively firmly attached to the inner surface of the prosthesis by fibrous-tissue pegs extending into the interstices of the graft (Fig. 6B). The graft was surrounded by a dense fibrous connective tissue. Although fibrous tissue had infiltrated the graft from the peri-adventitial tissue, it was interesting to note that once the specimen was opened longitudinally the surrounding tissue could easily be peeled off the outer surface of the

graft. Not all the spaces of the graft were filled with connective tissue but many contained extensive conglomerations of loose inflammatory cells (Fig. 7). No foreign-body giant cells were found. This was the same in all our cases, even if the graft had been implanted for many months. So far Y-shaped grafts prepared from Ivalon by the method described have been used in the treatment of 7 cases of aneu-

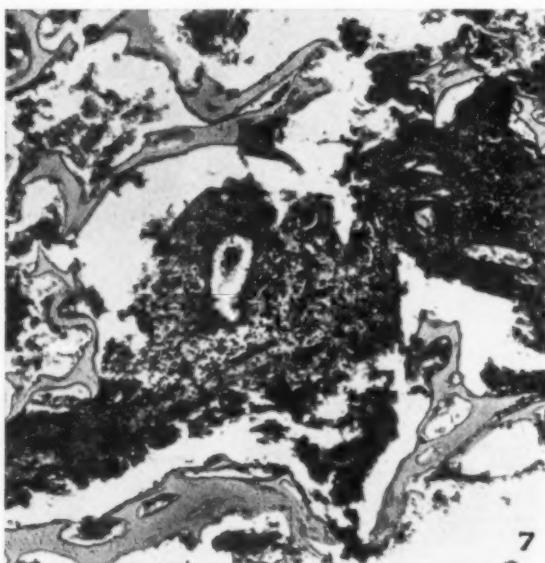


Fig. 7. Loose inflammatory cells in Ivalon spaces of graft.
Dog 11 months.

rysts of the abdominal aorta, 2 of which had ruptured before operation. The results will be reported in a separate communication.*

SUMMARY AND CONCLUSION

The justification for a more radical approach to the treatment of aortic aneurysms by means of excision and grafting is discussed.

The advantages of grafts made from inert non-biological material are listed, with special reference to grafts made from Polyvinyl sponge.

The method of constructing Y-shaped grafts from Polyvinyl sponge and Nylon net is described in detail.

Special attention is drawn to the importance of the correct proportions between the internal diameter of the terminal aorta and the iliac arteries of the graft.

It is suggested that this factor is of general importance when dealing with an elastic graft, and failure to pay attention to this point is thought to be responsible for many failures with Ivalon grafts in the past.

A post-stenotic dilatation is described in an Ivalon graft resulting from stenosis at the proximal suture line.

The histological appearances of grafts implanted for months are illustrated.

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Miss T. Merison and Mr. C. C. Goosen are responsible for the photographs and Mr. E. Martin for the histological sections.

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SCIENCE AND SHIBBOLETHS *

JOHN A. STALLWORTHY, F.R.C.S., F.R.C.O.G., F.A.C.S. (HON.)

Regional Director (Obstetrics and Gynaecology), Oxford; 1957 Guest Professor, University of Cape Town

Friend or foe?—this is the challenge, as yet unanswered, which science faces today as it stands on the frontier of tomorrow. Its claims to friendship are great. By its conquest of plague and pestilence, its contribution to social medicine, and its miracle

* A lecture delivered to the student-body, University of Cape Town, April 1957.

of modern therapeutics and surgery, it has prolonged the life of man. During the increased years it has given him it has raised the standards of his living and provided amenities, comforts and luxuries beyond his imagining even half a century ago. It has harnessed the powers of nature for man's benefit and is now learning to utilize the very elements from which the air, the earth and the sea are made. Electronic brains and automation are

introducing a new industrial revolution. 'But if thine enemy clothe thee and feed thee only to destroy thee in the end, his friendship is a mockery and by thy destruction he stands revealed as a mortal foe.' The threat of push-button warfare is now with us. Two bombs in the last War crushed a great nation. They devastated two Japanese cities and in their trail of desolation shattered the legend of centuries that Japan was the land of the gods and that, invincible and under a divine Emperor, she was destined one day to rule the world. In the chaos that followed, the Emperor denied his divinity and a legend died. But those two bombs which made such terrible history were as playthings compared with the modern weapons of international ballistic design which even now rest uneasily in the world's arsenals. If ever the command is given to dispatch these missiles of scientific annihilation it will also give the final answer to the challenge—friend or foe?

In thinking along these lines it may be that we are ascribing to science powers it does not possess and by so doing are perpetuating an age-long myth that the future of man depends on the developments of science rather than on Wisdom.

In the *Book of Judges*, Chapter 12, we read an account of the quarrel between the Ephraimites and the Gileadites. The men in these two tribes had so much in common that they could not with certainty distinguish one from the other. So it was that when the defeated Ephraimites were endeavouring to cross the Jordan and were caught by the Gileadites they knew they would be slain. They denied their tribe of origin and claimed that they were not Ephraimites. Their victors were cunning and asked them to pronounce the word *shibboleth*, meaning an ear of corn or a river. They knew the difficulty their foes would have with this word and those who said 'sibboleth' were slain. We can only hope that there were no lisping Gileadites who suffered this dire penalty for their infirmity. So it was that 'shibboleth' came to mean a password or catch-phrase. With the passage of time it has slowly changed its meaning to imply a catchword to which some people adhere long after any truth or significance it may once have possessed has disappeared.

Science and shibboleths: the terms may at first seem contradictory and, in an age when the prestige of science and its capacity for influencing the daily lives of men has never been greater, it may seem incredible that science and shibboleths should be associated. There are many even among those who are responsible for the educational policy on which the future of our race depends who believe so devoutly that in science is the hope of the future, that they would replace the study of the humanities by the technical training of scientific specialization. I believe that, if the thermonuclear weapons now delicately poised East and West remain leashed and there is a future for mankind, it will be revealed in the course of time that to hail science as all-powerful is itself a shibboleth.

SCIENCE AGE-LONG

We are told so often that we live in a scientific age, sometimes with pride by the scientist and sometimes with alarm by the ecclesiastic or the humanist, that it is refreshing to remember that Man has lived in such an age since time began. Developments in the past fifty years have been at a pace and of an importance far outstripping the progress of past centuries. But the ocean is still the ocean whether it be in the seclusion of a bay on a sheltered coast or in the mid-Atlantic. So it is with science. When our early primitive forebears first thought of making weapons for their defence or to secure meat for the larder, and fashioning implements, however crude, to till the soil—when they first looked at the heavens with wonder and observed the movement of the sun, the moon and the stars—the age of science dawned. Vast libraries have been written on its subsequent development, and so complex has science in all its ramifications become that no man living can be familiar with it all. In that fact, with its corollary of knowledge and ignorance walking hand in hand, there is fertile soil for the growth of shibboleths and it is not surprising that on occasions they should flourish like mushrooms, which also do well in the dark.

Bertrand Russell has said that 'knowledge is more often useful than harmful, whereas the fear of knowledge is far often more harmful than useful'. Had this dictum been accepted through the ages, the list of shibboleths associated with scientific development would be much shorter.

In the early accumulation of knowledge, which after all is the

object of science, Man studied the heavens. He assumed the earth was flat and the sky a dome which reached the earth at the horizon. The sun was a flaming chariot driven across the heavens by a sun-god and the clouds were heavenly cows which by celestial lactation, at times both appropriate and inappropriate, showered rain on the earth. These were concepts primitive man could understand and accept and before we laugh at his folly let us pause and make sure we are not of the many who still entrust our wealth to the stars by allowing business deals to be influenced by what the astrologer foretells in the daily press, or of those who entrust their safety to the charms attached to a bracelet, necklace or watchchain.

GRECIAN SCIENCE

The first civilization began in the valleys of the Nile, the Tigris and the Euphrates but it was four thousand years later in the Grecian age that the first scientific advances were made. This was the era of deductive reasoning and the first systematic attempt to understand the natural world. The Greeks reasoned that it was unthinkable that the earth could be supported in space as primitive man had imagined and therefore deduced that it must be floating freely. They appreciated that the moon reflected borrowed light and by their new mathematics they calculated its distance from the earth with remarkable accuracy. The school of Hippocrates in the 5th and 4th century before Christ amassed observations of great accuracy and recorded clinical experience so valuable that much of it is valid today. A high code of moral standards was enforced, revealing that human behaviour was considered important as well as the accumulation of knowledge. Would that these two concepts had progressed equally through the years! The shibboleth of that era was that deductive reasoning was the sole basis of science. Much of what had been learned was to be forgotten during the long years of scientific coma between the third and fifteenth century but, had there been a John Hunter in the school of Hippocrates to say to his fellow-pupil, Edward Jenner, on the island of Cos, as in fact he did in a letter in 1775, 'Why think, why not try the experiment?' the accepted infallibility of deductive reasoning would have been challenged and the scientific progress that would have resulted might well have transformed the history of the world. Two illustrations will suffice. The somewhat precocious but extremely intelligent seven-year-old son of an Oxford don, at that time head of a great college and now a Bishop in the Church of England, said to his mother, 'Is it true that when we are born we come from dust?' She replied, 'It is, my son.' He then said, 'Is it also true that when we die we go to dust?' and she replied in the affirmative. 'Well then, Mother', he stated, 'I wish you would look under my bed, for there is somebody either coming or going.' The reasoning seemed logical but the deduction was wrong. The Greeks had learned that when they travelled North it got cold and when they went South it got hot; so they deduced that the Arctic regions were lands of eternal snow, ice and darkness. It seemed reasonable but was not true. They could not be aware that more snow falls in Virginia than in certain areas of the Arctic lowlands, that the waters of those desolate Arctic regions are more richly inhabited than the tropical seas, or that light is no more foreign in the Arctic than in the tropics. That they were in error matters little, but the belief in deductive reasoning from which conclusions were drawn that were to be accepted for centuries was to be responsible for arresting progress. When the great philosophers made their declaration there was little scope for comment or criticism by men of lesser stature. Science and culture consisted of a knowledge of what famous men believed and taught, and much of it was not capable of proof. Scepticism is the life-blood of science and belief is the antithesis to thinking. It is not surprising, therefore, that the shibboleth of popular logic emerged which has persisted to the present day, namely the creed that if you cannot prove a thing is false it must be true. Such attitudes of mind can never be conducive to scientific progress.

THE ROMAN ERA

With the rise of the Roman Empire the culture and science of Greece became forgotten. True, Galen was the acknowledged master in the 2nd century and was popular in Rome, but dogmatic assertions are not evidence of progress. The spirit of science was stifled by scholasticism and doctrinal dispute, with the result that the age from the 3rd to the 15th century was a dark void in

human progress. It was an era of superstition. The earth was flat because the philosophers said it was flat and the Church endorsed the fact. Did not the Bible refer to the four corners of the earth, so how could it be anything but flat? To deny this was heresy. There were obviously heretics in those days as now, but heresy in this matter was easily dealt with by the deductive reasoning of the men of science. If the earth was not flat the water would run off it and where would the oceans be? If it were really spherical and revolving in space as some foolishly believed, the wind would always blow from East to West and an arrow shot into the air westward would fall behind the archer. As for the men who lived on it on its underside, did they have claws to keep themselves attached to its surface? The pure in heart knew this was not so for the Pope had confirmed that the earth was flat and the very fact that Joshua had made the sun stand still in the heavens confirmed the fallacy of these new beliefs. As Milton said later, 'Truth never comes into the world but like a bastard to the ignominy of him that brought its birth.'

During the Roman era the science of chemistry was born, but it was conceived in secret, greed and fraud with the avowed object of searching for wealth in the alchemist's stone. It did not prosper and for a thousand years the dark ages of superstition and false belief persisted. But the renaissance of science that was part of the glory of the 15th century was preceded by a renaissance of curiosity and the accumulation of new observations and facts. Whereas complacency breeds death, new ideas are always fertile fields for truth. The 15th and 16th centuries were the dawn of a glorious new era. In 1543 Copernicus and Vesalius exposed old heresies with new vigour and authority and advanced new concepts of thought but it was not for 300 years that it was admitted that the earth was round after all and revolving in space. No longer did the Church regard this as a belief flouting science and doctrine, for in 1820 Pope Pius VII declared that the Copernican system was established.

RENAISSANCE

Vesalius shocked the world and the professors of anatomy by dissecting the human body and revealing secrets hitherto concealed. True it is that dissection had been performed in Bologna as early as the 13th century and the new science had been used in the law when a professor was ordered to dissect a corpse to discover the cause of death, but the practice was not favoured and in 1300 Boniface VIII had issued a bull threatening with excommunication 'those who eviscerate the bodies of the dead and barbarously boil them in order that the bones separated from the flesh may be carried for sepulchre into their own country.' None the less, in the 15th century the practice of dissection spread more widely and Vesalius, Michaelangelo and Leonardo da Vinci all became skilled anatomists. Leonardo became so passionately involved that he created a new shibboleth. He believed that the answer to the riddle of life could be found in the substance of things material. He believed that in dissection he could reveal the origin of the primary and perhaps the secondary cause of their being. He wanted to work miracles but he scorned the alchemists and 'those would-be creators of gold and silver and engineers who would have dead water stir itself to life and perpetual motion'. Had he said heavy water instead of dead water his words may have been more prophetic! He was in search of ultimate truth, and in death he sought the answer to the mystery of life.

This was a century of famous men and it is understandable that in this renaissance of learning it was soon appreciated that science was a way to power. Leonardo was employed by the Duke of Milan because of his skill in designing fortifications and machines of war, just as Galileo in a later century aided the Grand Duke of Tuscany by his skill in calculating the trajectory of projectiles. It is interesting to note, however, that when Leonardo became engrossed in dissection and his search for the springs of life he no longer devoted his talents to producing instruments of destruction. Perchance with prophetic insight he already sensed the danger to which his application of science exposed mankind and realized the oak that could grow from so small an acorn. No doubt he believed then, as many believe now, that science held the key to power, but his actions would suggest that he realized the fallacy of the shibboleth that wealth and prowess in arms means power of ultimate value. He strove to find the secrets of life and ceased to be concerned with the alchemist's stone or the weapons of death.

An amusing instance of the influence of the Church on shibboleths and science is related to this period of history. Anatomical and biological studies were revealing the scientific significance of the umbilical cord and the navel. It was an era of great thinkers and deep thinking and it is therefore no surprise that someone conceived disturbing thoughts concerning the anatomy of Adam and Eve. The problem was whether or not they had navels. If they did it was obviously a useless adornment, not only of no scientific significance but positively misleading to future generations. It was argued by some that the Creator would not have been guilty of such an error while others argued that it might have been done deliberately to test the faith of the faithful as yet unborn. This was no musical farce, but a matter of great doctrinal and scientific moment. Adam and Eve were popular subjects for the great painters of that generation—and what great painters they were! These two historic personages were the equivalent of the famous film stars of the present time and the problem was whether to portray them with or without a navel. As far as the timid Eve was concerned it was easy for her flowing hair could so conveniently be caught by the breeze and leave the dispute unsettled. Adam was more difficult. Either he had the disputed article or he did not. It was not a traditional area for a friendly fig-leaf and so the result was inevitable. There were painters who included it, others omitted it. Michaelangelo declared at least his artistic faith by painting Adam and Eve in the Sistine Chapel under the very eyes of the Pope, or perhaps we should say over the very eyes of the Pope, with navels of generous proportions. Raphael included the same anatomical details in two pictures of Adam in the Vatican, so that tacitly at least the battle in ecclesiastical and scholastic circles had been won. This all sounds very ridiculous in this 20th century of grace, and yet as recently as 1944 a Congress committee in the United States of America opposed the circulation to American soldiers of a book entitled *The Races of Mankind* for the reason, among others, that it portrayed Adam and Eve with navels and there was no Michaelangelo then to paint the answer on the walls of the Senate House!

The respect with which science was regarded because of the powers it could confer on Man increased with the passing years. The 15th century saw the study of astronomy making great contributions to navigation, with all that this implied in the exploration of the new world and the bringing of wealth to the old.

Galileo produced the first astronomical telescope but, even more important, he had introduced a new technique to science, one which was to be the basis of the tremendous advances destined to revolutionize the life of Man in the years ahead. He combined the deductive reasoning of the Greeks with experiment, and with this twofold approach he studied the laws of velocity, inertia and acceleration. He introduced the lens, which made the telescope possible, and with it the new revelation of the heavens beyond the solar system. It also resulted in the development of the microscope, which was to reveal the mysteries in the minute, and biology with its roots in histology and cytology was born. In the 19th century Darwin and Mendel proclaimed their views on evolution and natural selection by the study of genetics. Physics came to the front in scientific progress with the discovery of X-rays, Dalton's description of the atom and J. J. Thomson's electron. Research in its modern concept of deduction and experiment was the tree which had grown from the seeds Galileo had planted long before. The great developments which were the forerunners of many greater in the 20th century were the natural outcome of the new technique. Scientific research implies the ability to plan and to criticize, to recognize limitations and to investigate sources of error and, above all, to accept the basic concept that conflicting evidence is as important and may be more important than evidence which supports a theory. In short it demands intellectual integrity of the highest order and not all men have this quality. This is the reason why the very word research has all too frequently come to be a shibboleth, probably one of the greatest shibboleths in the history of science.

RESEARCH

Research has played and must continue to play a vital part in scientific progress, but that magic word 'research' is often a shibboleth. It can be a password into scientific and pseudo-scientific departments, an open sesame to trust accounts dedicated to scientific advancement, an excuse for incredible waste of time and money, and a nom-de-plume for much that is neither scientific

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original. Because of the returns which industry has reaped from scientific development and because of the still greater rewards we can expect in the future, it is natural that vast sums of money should be set aside to encourage research. This is commendable, but business by the very nature of its existence expects its invested capital to produce more wealth. So we have applied or industrial research as opposed to pure or basic research. The pure scientist, generally speaking, retains his purity by working in a University laboratory, where he is more interested in searching for truth for truth's sake than he is in the material rewards that might result from any discovery he makes. The applied scientist, on the other hand, generally conducts his research under the patronage of industry. Both have made great contributions to Man's knowledge. One thinks of the famous Cavendish laboratories, founded in 1871, and pauses to pay tribute to famous men such as Rutherford and his illustrious successors for the gifts they have given to science and to Man. One recalls also the painstaking care and attention to infinite detail with which the loss of a Comet aircraft was so fully investigated and from the lessons learned in this disaster sees how applied research has been used to safeguard the mighty aircraft of today and tomorrow. It would not be unfair to claim that industry is more jealous of results and preferably positive results than is the typical University hierarchy in scientific matters. In 1830 Sir David Brewster said, 'Can we behold unmoved the Science of England struggling for existence, the meek unarmed victim of political strife?' and the following year at York the British Association for the Advancement of Science was founded. One result has been increased facilities for the training of scientists, a necessary feature in a highly technical age. Too often the relatively untrained worker, untrained, that is, in scientific methods, is attracted by the 'allure of research' into projects which in terms of ultimate knowledge are unfruitful, and all too often his success is estimated by the number of papers he has published rather than by the scientific worth of the work he has done. Medicine has attracted more than its share of this type of research worker. An encouraging development for combating these dangers has been the institution of research boards and research councils to guide and advise on these matters.

FREEDOM

The shibboleth that secrecy is essential to research is responsible for much that has been wrong. More open discussion with men of alert and critical minds would reveal fallacies before they were perpetrated in treatises or oration and would indicate new possibilities worthy of exploration. It is not always easy for Man to appreciate the fact that the truth is more important than the name of the worker who discovered it. A splendid illustration of the free interchange of ideas occurred at the end of the 18th century in Great Britain, when the celebrated Lunar Society flourished in the Birmingham area. Three men, Erasmus Darwin, grandfather of Charles Darwin, a physician and poet, William Small, physician and chemist, and Matthew Boulton, industrialist, engineer and chemist, founded it. This nucleus attracted men of distinction from further afield and these included Priestley, James Watt, Baskerville, Sir Joseph Banks, President of the Royal Society, and Smeaton, the builder of the Eddystone lighthouse. They met once a month on the Monday nearest the full moon and for this reason were named 'The Lunatics', by the butler at one home at which they met. Priestley discussed his work on oxygen on these occasions and James Watt's steam engine was developed by the discussion and free interchange of ideas and criticisms which were a feature of their monthly meetings. The Society was disbanded by rioters in 1791 when, crying 'No phil-

osophers—Church and King forever', they burnt homes, destroyed instruments, ruined libraries and in the cause of freedom once more arrested Man's progress, this time fortunately for only a short space of time. The shibboleth that philosophy and science are the enemies of religion and the Church was responsible for the unhappy interlude. Freedom to think can mean nothing without freedom of speech and of action and freedom of thought cannot exist without encountering doubts. Doubts are always disconcerting, but from grappling with them new ideas are born and the truth may be discovered. The shibboleth 'Science says' or 'The scientist has shown' are usually popular misconceptions accepted by the ignorant; as for example the belief that lightning never strikes in the same place twice—the Empire State Building in New York was struck 68 times in the first ten years of its life—or that natural childbirth is every woman's birthright. It is the heritage of the bird to fly but many a fledgling falls to its death in the effort to achieve this, just as many a young seal is drowned when learning to swim.

Through the centuries Man has achieved great things, but in spite of this his peril has never been greater than it is today. Discoveries of glorious potential have been prostituted by political tyranny—and the basis of all tyranny is fraud. For it is the weapon dictators and tyrants wield with great effect in the small spheres of life as well as in major national and international disputes. Shibboleth or science can both be used to further this purpose. In the primeval marshes and swamps the dinosaurs reigned supreme but, when the swamps dried up and the environment changed, through no effort on the part of the dinosaurs, they perished because they were unable to adapt themselves to the new environment. Man has changed and is changing his world by the powers of his own invention and ingenuity, but he has now to prove that he can adjust himself to his changing scenes. Unlike the dinosaurs he does not need a physical readjustment but one that will be intellectual, moral and spiritual. If he fails, the history of the dinosaurs may be repeated. It will not be in science that the answer to this great problem will be found, but in Wisdom. Leonardo sought in vain amid the delicate perfection of nerve and vessel for the answer to the riddle of life. Science in its relatively new fields of psychology and psychiatry is also struggling to find the answer. Where then can Wisdom be found? While I was pondering on these things some weeks ago I went to Evensong in the lovely chapel of Magdalen College, Oxford. The fact that for four hundred years dons and students, commoners and princes, had gathered here to worship without regard to race or colour gave a sense of timeless beauty to the scene. As the shaded candles cast their soft light on the high vaulted roof with its delicate stone tracerу, the golden-voiced choristers rose to sing an anthem based on a passage from the Book of Job and in the loveliness of their song provided the answer for which I was seeking:

'But where shall Wisdom be found?
And where is the place of understanding?
Man knoweth not the price thereof;
Neither is it found in the land of the living.
The deep sayeth it is not in me
And the sea sayeth it is not with me.
It cannot be gotten for gold,
Neither shall silver be weighed for the price thereof.
Whence then cometh Wisdom?
And where is the place of understanding?
Seeing it is hidden from the eyes of all living and
Kept close from the fowls of the air.
Behold the fear of the Lord that is Wisdom
And to depart from evil that is understanding.'

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THE NATURE OF THE PSYCHOPATHIC PERSONALITY: SOME OBSERVATIONS*

DAVID PERK, M.D., D.P.M.

Part-time Senior Neuro-psychiatrist, Tara Hospital, Johannesburg

An attempt is made in this paper to throw light on the nature of the psychopathic personality, especially in regard to its aetiology.

Definition. I define psychopathic personality as a personality presentation which represents or reflects a chronic maladjustment, unaccompanied, by and large, by a feeling of self-criticism or lasting distress, unassociated with any apparent cause, and generally speaking—depending on the gravity of the condition—not susceptible to treatment or punishment.

Instability is a characteristic of early life, and stabilization is a development which follows the selection, unconscious and conscious, of patterns of thinking, feeling and behaving appropriate to the culture and milieu of the individual. Two sets of circumstances prevent such an evolution; one, where the inherited predisposition to instability outweighs the stabilizing influence of environment and experience, and the other, where the environment and experience is itself psychopathic and traumatic, so that the individual does not even get a chance of stabilization. In either case instability precedes psychopathy. This is the reason why the diagnosis of psychopathic personality is not commonly made in connection with the emotional, character and behaviour disorders in early life. They are regarded, according to their gravity and aetiology, as being either of a reactive or a psychotic nature. The plasticity and instability of the child permits of endless changes in behavioural pattern, and it is not until adolescence is reached that one begins to feel that the patterns are becoming organized and established. It is at this stage that one can use the diagnosis of psychopathic personality, where it applies, though with caution, in inverse proportion to the age.¹

The development of the psychopathic personality generally takes place before maturity, though it may occur in adulthood. In the former case, it becomes progressively more manifest as the life situation of the individual becomes increasingly testing and challenging with his growth; in the latter, the appearance is more sudden and is frequently preceded by some catastrophic experience. In both cases the cardinal feature is that the individual accepts his failure of adjustment without anxiety or guilt, and therefore without any acute recognition of failure. The challenge of the environment may cause a measure of distress, it is true, but the psychopath does not, to any adequate extent, feel the fault or difficulty to lie within himself, so that he feels no conflict and no call to change himself. He carries on, disregarding the disapproval or condemnation of society, unless and until he is stopped by the self-protective and retaliatory measures of society.

The psychopath presents a warped and restricted ego and a feebly developed, absent, or non-functioning super-ego, so that he is free of conflict, and suffers in consequence none of its acute and lasting distress. The psychopath frequently has a poor intellectual endowment, but not always. The better the intelligence of the psychopath the less likely is he to flout the law flagrantly, but this enables him to find more victims amongst the trusting and unsuspecting members of the community.

Maladjustments, more or less asymptomatic, i.e., where the patient senses very little wrong with himself whatever pathological manifestations the observer may detect, are seen in a number of conditions other than psychopathic personality. They are (a) transient situational reactions, (b) psychotic states, (c) organic brain damage, and (d) personality changes associated with illness, chronic infection and intoxication, endocrine dysfunction and certain somatic disorders.

These conditions have to be excluded before the diagnosis of psychopathic personality can be made. It will be seen that they fall into 2 classes, viz. those conditions that are not accompanied, as far as we know, by any cerebral or bodily pathology—this class comprises the transient situational maladjustment and the idiopathic psychotic states—and those that are based on organic cerebral change or bodily pathological conditions. In either

class the psychopathic presentation may be acute or chronic, transitory or enduring. If transitory, the ephemeral nature of the condition confirms that the disturbance of the personality is extrinsic to its essential structure; with true psychopathic personality the psychopathy is part of the organized, developed personality, essentially unchanged by the passage of time. If chronic, the psychopathy may be seen to be part of a more extensive symptom-complex, which affects the personality in a way that stands out in marked contrast with the pre-morbid personality. A history of cerebral injury or disease or severe bodily condition calls for consideration of the possibility that the psychopathy may be secondary to this injury.

Two observations are inspired by the simulation of psychopathic personality by certain other conditions. One is that if an organic change can produce a condition that is identical with the one that has no discoverable organic background, i.e., with psychopathic personality, reserve concerning the possibility that improvement in our investigational techniques might lead to the discovery of a physical factor in the latter class, is surely not unwarranted and, conversely, that the presence of a physical factor in the former class does not negate the operation of emotional causes. The other is that there would seem to be a link between psychopathic and psychotic states, in that they can both result from a frank organic disturbance.

Conditions which mimic the psychopathic personality

To give a clearer picture of what psychopathic personality is not, it may not be out of place to give a little detail of the conditions which mimic it, and from which it has to be distinguished. These include:

(a) Transient situational reactions, i.e. reactions to a gross physical or emotional stress, or to a situational challenge. The manifestation will vary with the stage and character of the development of the personality. The child will manifest a change of pattern of behaviour and social response, or a regression to discarded earlier habits, or the formation of pathological traits. In adult life, it may take one of numerous forms of which the commonest are passing maladjustments (evinced by anxiety, restlessness, lowered morale, lowered efficiency, alcoholism, lowering of sexual restraint), excitable response, dependency reaction, passive-aggressive reaction, aggressive reaction, panic reaction, paranoid reaction, drunkenness, hysterical twilight state, Ganser state.

(b) Personality changes associated with organic brain disorders, such as brain injury, encephalitis, epilepsy, disseminated sclerosis.

(c) Personality changes associated with bodily disturbance, such as spes phthisica, longings of pregnancy, changes accompanying exophthalmic goitre, myxoedema, hypertension, jaundice.

Classification

Considering that we are dealing with a long-standing, if not life-long, maladjustment, the basis of classification should logically embrace a reference both to the degree of maladjustment and to its clinical features. The degree of maladjustment of necessity reflects the reaction or judgment of society on the individual. I therefore suggest the following as a suitable classification:

(a) Misfits: inadequate personality, schizoid personality, cycloid personality, paranoid personality, epileptic character, cranks, sexual deviants

(b) Sociopaths: alcoholics, drug addicts, aggressive psychopaths

(c) Social pariahs: vagrants, hermits, prostitutes

(d) Criminals

AETIOLOGY

The aetiology of psychopathic personality may be considered from two angles: firstly that of the predisposition to the formation of the particular type of personality and, secondly, that of the precipitation of overt manifestations of the incapacity to conform and appropriate behaviour which is latent in the personality structure. Psychopathic personality embraces two historical dimensions of the personality, viz. the long term one, presenting

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a precarious balance that betrays the individual's inability to cope with his environment realistically, and the episodic one, 'highlighting,' in acute disturbances, the instability of the personality.

Predisposition is the result either of inherited constitutional instability or the ultimate effect of cumulative life experience, or of both factors. Depending on the bias of the clinician, there is frequently a disposition to argue in favour of one or the other causation. But rationally approached, it must be recognized that they are not mutually exclusive, that there is very frequently evidence of the existence of both factors in this condition, and that in many cases the disturbing environmental influences flow from the heritable instability of the parents responsible for the environment. It may be possible in any particular case to divide responsibility, in a rough way, between the constitutional and the environmental factors, according to their prominence, but to blame the more prominent factor is no excuse for denying the existence of the other. It is important to bear in mind that genetic influences may long remain latent, and in addition may require, for manifestation, the impact of a suitable dovetailing environmental stress.³

What is the evidence for the presence of an inherited or genetic factor in the production of psychopathic personality? I would advance the following: (a) The evidence that disturbance of the brain, as by disease or injury, can produce a condition identical with psychopathic personality. It is surely deducible from this that cerebral patterns which reflect genetic influences can have the same effect. (b) The excessive proportion of psychopaths found in the near relations of psychopathic personalities. (c) The excessive proportion of psychopaths found in the near relations of psychotics.³ (d) The comparatively early age at which the condition becomes observable. (e) The frequent association between psychopathic personality and mental defectiveness.

Genetic and environmental influences may not supply the whole answer, after known cerebral injury or disease have been excluded. Much remains to be established concerning the effect of (i) intrauterine events, such as injury and infection, (ii) cerebral injuries at birth, short of producing gross neurological lesions and intellectual deficiencies, and (iii) asymptomatic cerebral injury and infection in the early years of life. May these events not account for some of the psychopathic personalities? May they not account for some of the abnormal electroencephalograms found in a relatively high proportion of the cases?

No one who has taken histories of cases of psychopathic personality can help being struck by the frequent occurrence of grossly abnormal home environments in the early lives of these cases. I would go further: it is almost inconceivable that a psychopathic personality could have had a normal early life experience. That does not, of course, mean to say that a normal early home life necessarily produces a normal person, nor that an abnormal one necessarily results in an abnormal personality. A psychopath and a normal early upbringing are inconsistent. It is clear enough that a diagnosis of psychopathic personality could not be inferred from an abnormal early upbringing, but equally there is no good ground for dismissing the importance of this factor on the basis that normal personalities have been known to emerge from such a background. The most, surely, that can be read into the fact that both normal and abnormal personalities are consistent with an abnormal early parental and home influence is that this factor is not the only determinant operating in the production of psychopathic personality. The answer, no doubt, is to be found in the combination of genetic and environmental influence, and in the latter must be included the prenatal, natal and immediately post-natal events to which I have referred above. With an open mind and careful enquiry there is little difficulty in detecting the presence of the two influences, and it is found that in some cases one or other influence is the dominant, and in others the two play more or less equal roles.

Before passing on from the subject of the relationship between abnormal environmental influences and abnormal personalities I should like to make two observations that I regard as axiomatic: firstly, that where the early home influence is grossly abnormal the child reared in it cannot escape unscathed and, secondly, that where an abnormal personality is historically associated with an abnormal background the two are aetiologically related. The relationship, as I have explained above, does not of course exclude the operation of other factors, such as genetic and cerebral damage.

It will have been noted that in the first observation I referred

to the effect *on the child*; this effect cannot reasonably be denied in such a context, or we are reduced to the view, palpably absurd, that the child is ineducable. But if the child is affected by the abnormal early home influence, what can intervene to make adult personality less related to it? There is, firstly, the plasticity of the individual, the innate capacity for adaptation. When, however, one considers that an inherited instability, as evidenced by the history of instability in other members of the family, is almost invariably present, though it may not always be in a dominant role, it is evident the combination of early damage to the personality plus constitutional instability is likely to outweigh plasticity. Plasticity, in any case, does not so much imply capacity for correcting early patterns of behaviour as their integration or incorporation in later patterns, and if the earlier ones are wrong the later ones are likely to be wrong likewise. The important consideration, however, is that plasticity is present in inverse proportion to constitutional or inherited instability. Secondly, there is the change that comes to the early home atmosphere with the aging of the parents, and the change of circumstances that comes with time, in the parental home and beyond it. I do not believe that they substantially affect the earlier patterns of response. In short, the word 'child' can be omitted from the first observation, so that it reads as follows: where the early home influence has been grossly abnormal the personality emerging from it is unlikely to be normal.

To summarize, psychopathic personalities fall aetiologically into 3 classes, viz. (a) mainly inherited, where the genetic influence is dominant, (b) mainly acquired, where the environmental influence (life experience or cerebral damage or both) is dominant, and (c) partly inherited and partly acquired.

Factors promoting manifestation of instability

We can now turn to a consideration of the influences or factors that provoke a manifestation of the instability latent within the psyche. They are, firstly, the impact of a stress, secondly, the challenge of the environment and, thirdly, the discharge of psychic tension that keeps building up. All these presume a degree of susceptibility to stress.

Maladjustment, which is the cardinal feature of psychopathic personality, implies not only an adjustment to the individual's environment, albeit a poor or bad one, already established, but an incapacity to adjust. The former represents the static limitations of the personality, the latter the dynamic relationship between the individual and his environment; or, stated differently, the one defines the psychopathy, the other reveals the instability. Incapacity to adjust must mean that the affected individual finds an environment, innocuous to the normal person, stressful to himself; and it is this undue susceptibility to stress which is the essence of instability.

The frailty and dependence of early life must necessarily make the young child susceptible to stress, and the more abnormal the early environment the more stressful it must prove to the child. If to the influence of a stressful environment acting on the normally susceptible child is added the susceptibility that derives from an inherited instability, an abnormal environment must be particularly stressful to the constitutionally predisposed child.

Early experiences, if uncorrected, sensitize the individual to later stresses and establish patterns of over-sensitive or pathological response to them so that, as the individual advances in years, his environment becomes more capable of disturbing him, unconsciously if not consciously. How far an inherited instability keeps company with an individual it is hard to say, but the mischief it effects early in life is enough to influence an individual for the rest of his days, without continuing to operate into adulthood.

The responses in childhood to sustained stress must necessarily involve sacrifice of the personality, because if the environment is so abnormal as not to yield to its needs, the child certainly has no power to change the environment. The sacrifice will ease the stress but increase the sensitivity to it, and it is these buried or unconscious susceptibilities which make the psychopathic personality so sensitive to his environment as not only to over-react to minimal stress but frequently to behave as if the stress were always there, even if it is not apparent to others. By the same unconscious route he may evoke pathological patterns of behaviour in response both to instinctual urges and environmental promptings.

The psychopathic personality evinces a maladjusted response to stress in anticipation of it, in the face of it, and in retrospect. In anticipation he feels a far greater threat than is objectively

warranted and he may rationalize, almost to the point of delusion, to support his emotional response. The distress engendered is not sustained, because as he feels the threat so he takes action, and the line of action follows the individual pattern of the psychopath (that is to say, it may be evasive or aggressive or pathological); but it always represents an unrealistic or extravagant reaction to a situation. The psychopath has little tolerance of stress, whether in anticipation or in actual experience of it. The anguish that comes from a long drawn-out conflict between ego drives and super-ego restraint is not experienced by the psychopath. His distress derives, in the main, from excessive aggressive drives or frustration. The greater the susceptibility to stress, the greater the distress engendered with the impact. In the face of threat the response comes even faster and is therefore apt to be more bizarre; in retrospect there is no regret, remorse or fresh alignment.

Influence of Environment. Because the susceptibility to stress is partly inherited, and therefore presumably operative from birth, and partly the product of early life experience, the individual who is the victim of these influences, i.e. the psychopathic personality of later years, is an easy prey to environmental stresses. So that, in a manner of speaking, the psychopathic personality is an artifact of the environment. That is not to say that the fault is with the environment, but that with a highly susceptible individual the disturbances he experiences frequently reflect in a very sensitive manner the demands, moods and judgements of the environment in which he lives. And as different environments have different standards, psychopathy may, in a sense, be said to be the product of environmental differences. In other words, a pattern of behaviour is no more psychopathic than a particular environment considers it.

When one considers that psychopathic personality is essentially asymptomatic and that it represents a disposition to react ineffectively, aggressively, or pathologically to society, it is not surprising that psychopathic personality presents itself more often as a social than as a clinical problem. Welfare organizations on the one hand, and the police on the other, deal with most of the psychopaths in the community. The medical man sees comparatively few of them. It is only when a large section of the community comes under enforced supervision and discipline as, for instance, in a war-time army, that the psychiatrist receives the opportunity of meeting the psychopaths in the community.

A rigid institution like the army shows an intolerance of some aberrant patterns of behaviour and a greater tolerance of others. It is, for instance, apt to close its eyes to excessive drinking, and yet is very sensitive to the least manifestation of overt homosexuality. In some oriental countries, which observe the purdah and strict abstinence from strong drink, overt homosexuality is permissive and drinking is forbidden. The greater the tolerance a community displays towards a failing, the greater its ire when it is overstepped, and in its vengeance it turns to the law to mete out punishment rather than to the psychiatrist to attempt correction. Where there is less tolerance, society's response is to reject rather than to punish. In the army, the homosexual was quickly referred to the psychiatrist for boarding out. The result is that army figures for psychiatric conditions show a low rate for alcoholism and a relatively high one for other forms of psychopathy, including homosexuality. In civilian life, on the other hand, the alcoholic occupies the prime place in the list of psychopathic personalities seen by the psychiatrist. But, as I have already indicated, that is no criterion of the incidence of the various types in a civil community, because other organizations in the main deal with the other types. Again, in the rigid discipline of the army the timorous, inadequate, unstable and aggressive personalities have little scope for manoeuvre; in civilian life there is much more scope for adjustment at individual levels, and concealment is aided and abetted by family pride. Incidentally the contrasting responses to alcoholism and homosexuality, to which I referred above, are not without significance; alcoholism may mask homosexuality.

DIFFERENTIAL DIAGNOSIS

On this subject I shall confine myself to a few general remarks. The differentiation between psychopathic personality and psychoneurotic states rests essentially on the presence of conflict and anxiety in the latter, and its relative absence in the former. In the chronic states, where various mechanisms are brought into play to relieve and canalize the anxiety, there may be so much masking of the anxiety that a close resemblance to psychopathic personality may be created, and if enquiry does not elicit a con-

fictual basis for the condition, of if the behaviour of the individual is grossly disordered, the condition may well be regarded as that of psychopathic personality.

Superficially, there appears to be a good deal of similarity between psychopathic personality and psychosis. They both present pathological behaviour patterns and both have reduced insight, though it is more pronounced in the psychotic. Their distinction is based on the following: that in the psychopath the sensorium, except for fleeting moments, is unimpaired; that extreme mood changes, when they occur, are transitory; that intellect is never more than momentarily impaired; and that affectivity, though altered, is not dissonant to ideation. The moral sense and self-esteem are defective in the absence of delusions. It will be appreciated from this that there are moments when the psychopath is psychotic.

The question of insight calls for comment. Just as insight is present, qualitatively and quantitatively, in degrees that vary from one normal individual to the other, it is also reduced in degrees that vary from one pathological personality to the other. We are acquainted with the absence of insight that is more or less the rule in established psychoses. The poverty of insight in pathological personality types does not, as a rule, go as far as that, but, generally speaking, insight is reduced. The more pathological the personality the more reduced is the insight. To some extent insight or the reduction of it will vary with the age at which the pathological personality type becomes established and with the length of time it has taken for establishment. Where the constitutional or innate predisposition is pronounced, the establishment of the psychopathy may be affected early in life unless the plasticity of the individual has delayed its establishment and, generally speaking, the earlier in life the condition is established and the longer its duration, the less the insight.

Is every irresponsible and antisocial act and crime psychopathic? Is every criminal a psychopath? The answer depends on the combination of a number of considerations. The first is that of motive. If the act, in its effect, is devoid of any thought for others, or if it is positively antisocial, it is of course psychopathic, whatever good the individual may claim for it. If the claim of a good goal is designed to camouflage an antisocial motive it makes the act doubly psychopathic; if it simply betrays the ignorance or stupidity of the individual, his response to the social disapproval or condemnation it provokes will indicate to what extent the act is psychopathic. Acts committed under the influence of psychotic ideas and feelings or some sweeping mass sentiment or emotion fall outside the frame of reference supplied by the term 'psychopathic'. It is not only by the end-result that the act must be judged, but also by the means used to achieve it. The means may, in part or whole, be antisocial, and therefore psychopathic, and yet the end-result may be good. The law will punish a man for stealing food for his children, but it would depend on circumstances whether the act could be regarded as grossly psychopathic. On the other hand, I dare to think that no end can be good where the means are outrageously bad.

The third consideration ('circumstances', referred to above, being the second consideration) is the presence or absence of anxiety and guilt in response to social disapproval. If the individual is undisturbed by disapproval of his act, it has the hallmark of the psychopathic. The last consideration is the long-term pattern of behaviour. The repetition of psychopathic acts sets the stamp on the psychopathic personality. A single crime may not point to psychopathy, but recidivism does.

To what category does a man belong who, by a series of callous swindles, which have evaded detection by the law, becomes rich, and then uses his riches for the public good? I ask this rhetorical question to bring out, firstly, how important it is, for escaping the label of psychopathic personality, not to be discovered and not to fail, whether by skill or luck, and, secondly, that psychopathy may be a reaction to a specific influence and disappear with it.

This may be an opportune moment to mention some of the outstanding features that characterize the aggressive type of psychopathic personality. They are, essentially, five, viz. (a) An inadequate appreciation of a moral duty and a moral veto, (b) an inadequate impact on conscience of immoral conduct, (c) an intolerance of frustration, (d) a relative absence of resistance to the demands of self-satisfaction and vanity, and (e) an aggression that gives motor power to the egotistic and egoistic drives.¹

The relationship of epilepsy to psychopathic personality is an interesting one, and may provide an important key to the elucidation

of the epileptic personality. Few do so. It correlates with the advanced medication. The disorder is mainly that of the central nervous system. Instability, psychopathology, changes being found among relatives of the patient, but that the instability is mainly conceive.

It is possible that the person has other psychological cases of abnormality with psychopathology.

It is not difficult to find life experience. Moreover, leaves the normal between question in a psychological discovery which he thinks best, whom it drives are ways.²

One of The higher standing predication where 'e' Burt has tendency emotional likely to be.

From the sense and the strength or from drives are who fail thinking to 'good' satisfaction fear of want of the super moral authority that provides in a criminal in the past need the need individual to punish

individual as that similarity they both reduced their psychopath; that history; that and that on. The delusions, when the insight is that vary reduced in the other. more or insight in as far as were patho- To some the age at established it. Where once, only in life establishment established psychopathic? is on the past is that is sought for psychopathic, claim of a it makes ignorance or approval extent the influence of sentiment caused by the act it. The psycho- will punish depend on my psychopath can be above, presence of individual hall-mark long-term facts sets time may of callous becomes rich. rhetorical escaping and not to psychopathy with the type of . (a) An o. (b) an . (c) an instance to aggression .¹ It is an elucidation of the nature of psychopathic personality. Not all cases of epilepsy develop character features that, in combination, are the unmistakable hallmark of the epileptic. In fact, comparatively few do so. In these cases the degree of character deviation developed correlates with the number of fits taken. Various explanations have been advanced for this, such as the influence of anti-convulsant medication, the traumatic effect of fits, the progressive nature of the disorder, but I should like to present another point of view, namely that epilepsy reflects an instability of the higher centres of the central nervous system, that the occurrence of fits and the development of psychopathy are both manifestations of the instability, and that the incidence of the fits and the degree of psychopathy are measures of it. Many epileptics show personality changes before the onset of fits, psychopaths are frequently to be found among the relatives of epileptics,² and epileptics among the relatives of psychopaths. These observations support the view that the relationship is not directly between fits and psychopathy, but that the link is through a common causality, namely the instability of the higher centres. What is the derivation of this instability? As I mentioned earlier, it can be either mainly inherited or mainly acquired or both. An inherited instability, it can hardly be conceived, could escape the super-addition of an acquired one.

It is possible to grade cases of idiopathic epilepsy and psychopathic personality in a series culminating in two extremes. On the one hand there is epilepsy without psychopathy and on the other psychopathy without epilepsy. In between there are the cases of epilepsy of varying severity, from the presence of an abnormal EEG to the severest epileptic manifestations, associated with psychopathy of different degrees.

PSYCHOPATHOLOGY

It is not difficult to recognize the link between an abnormal early life experience and an associated malformation of the personality. Moreover, it can hardly be imagined that abnormal experience leaves the personality unaffected, or that a morbid personality is normal but is preceded by abnormal experience. If the equation between experience and personality is so complete, what, the question arises, is the contribution made by inherited instability, in psychodynamic terms? I think the answer may lie in Burt's discovery of a general factor of emotionality or strength of instinct, which he calls "e". An individual in whom "e" is strong will, other things being equal, be more prone to delinquency than one in whom it is weak; he will require a greater measure of control (internal or external) if his generally more powerful instinctive drives are to be prevented from finding expression in anti-social ways.⁴

One of the inherited internal controls is that of intelligence ("g"). The higher the intelligence the better the perception and understanding of moral issues and, though this does not necessarily predicate moral discipline and restraint, it does exert that influence where "e" is not so strong as to overwhelm restraints. In addition, Burt has linked up the development of delinquency with the tendency of individuals to incline to either sthenic or asthenic emotional expression. The sthenic ones, in his view, are more likely to be associated with delinquency.

From the Freudian standpoint, the failure to develop a social sense and to achieve an adequate social adjustment derives from the strength of the id impulses relative to that of the super-ego, or from the weakness or corruption of the super-ego. Egoistic drives are encouraged and strengthened by over-indulgent parents, who fail to inculcate self-restraint and social discipline, by unthinking and loveless parents, who are so unalive or unrewarding to "good" conduct that it offers no inducement against egotistic satisfactions, or by over-severe and harsh parents, who instil a fear of wrong-doing but not a love of right conduct. The failure of the super-ego to develop adequately arises either from the weak moral authority of the parents, or from a tyrannous authority that provokes rebelliousness. The super-ego may become corrupted by an ego-ideal which over-compensates for deficiencies or inferiorities in aggressive and exhibitionistic behaviour, which may be criminal in character, or by the introjection of the immoral patterns of the parents.⁴ It may develop a criminal orientation from the need to seek punishment, inspiring the commission of new crimes, the need to relieve the guilt of past ones, real or imagined, or the need to seek justification in retaliatory aggression for the individual's own aggressive impulses, or from the provocation to punish by projected guilt, or from the urge to self-assertion and

revenge aroused by the feared and hated father or rival sibling.⁴ The more abnormal the personalities of the parents are, the greater the danger to their offspring of being left stranded in an inadequately resolved oedipus relationship to them. The consequent hatred and fear of the father induces guilt, which invites failure in life and social punishment, and the father's personality fails to be adequately introjected, so that the super-ego remains stunted. The individual is thus unconsciously directed towards goals that are destructive both of society and of himself.

TREATMENT

Reference has been made in a preceding paragraph to the aetiological parallelism between psychopathic personality and psychotic states. There is a further resemblance in their common insusceptibility to the psychotherapeutic approach. Leaving aside the organic reactions that are included in the psychotic states because in these the basic anatomico-physiological foundation of the personality is altered, what features of the psychical make-up does psychopathic personality share with psychotic states, to account for this common therapeutic characteristic? Susceptibility to psychotherapy depends essentially on the presence of two psychical features, one insight and the other a capacity for transference. They are, of course, relative measurements, but in the absence of such a degree of insight as will enable the individual at least to recognize that there is something wrong with himself and, further, in the absence of any ability to project onto another person the imagos that reside within the super-ego, he cannot but be insusceptible to psychotherapy. Without entering into a detailed dissection of insight and transference, it is possible to postulate that their functioning depends on the presence and action of the super-ego. The super-ego is the unconscious standard by which the individual is, and feels, constantly under judgment in his design for, and actual, living. It is understandable therefore that in its absence the individual has no check on himself and no means of feeling or knowing that all is not well with himself. Equally he has no mooring rope with which to fasten on to another human being. It is because the psychopathic personality and the psychotic individual operate in the absence of a properly functioning super-ego that they are not amenable to psychotherapy. We have already indicated how and why the super-ego fails to develop adequately in the psychopathic personality. In the psychotic state the balance between super-ego and ego is destroyed, to a greater or less degree, temporarily or more or less permanently, so that there is in effect no normally functioning super-ego.

The theory outlined above fits the general experience with psychopaths that they are by and large beyond reach and help. In his episodic disturbances, which are frequently reactive in character, the psychopath may be ready enough to be assisted. He wants an ally in his fight with an obstacle or stress, but on his own terms. And even if he makes some concession to the objective standpoint of the therapist, it is tentative and temporary and with an eye to the immediate purpose of dealing with the stressful challenge to his advantage. Once the crisis is over, he has no interest in the therapy or therapist. It is this unhappy characteristic which gives this diagnosis such a forbidding character and such a poor prognosis, and it is for this very reason that it should be used with due caution.

Psychotic states are, in a way, in a more favourable position, therapeutically. Physical treatments, such as insulin and ECT, have changed the prognosis in these conditions in a revolutionary way. In view of the close association between psychopathic personality and organic cerebral disturbance, as in epilepsy and disease or injury of the brain, the question of a physical approach to psychopathic personality becomes pertinent. Leucotomy has been performed for some time in cases of psychopathic personality and my impression, from reading some of the literature on the subject, is that it is not without value, especially in the case of the inadequate and schizoid types of psychopathic personality.⁵ Since 1952 there has been available a steroid (dehydro-iso-androstone) with the trade name of Diandrone which, the manufacturers claim, promotes aggression, self-confidence and masculine activity. From this, Sands and Chamberlain⁶ claimed useful results in the inadequate type of psychopath, the benefit disappearing with withdrawal of the drug. Chlorpromazine, it is claimed, helps the adjustment of aggressive children and youths by controlling destructive and hostile impulses. The association of epilepsy with psychopathy has naturally led to the use of anti-convulsant

medication in such cases. Where the psychopathy is part of the epileptic character I cannot recall that the control of the fits has had more than a passing influence on the personality of the epileptic subject. Where, however, the psychopathy is a parallel, but unlinked, manifestation, the exhibition of the anti-convulsant drugs is either without any real effect—the sedation may produce an apparent improvement, but it exerts no basic or permanent influence—or it may provoke a psychotic reaction. I must hasten to add that the latter observation is based on a single experience we have had at Tara. The patient (Mrs. D., aged 30) with a long history of anti-social and irresponsible behaviour, gross emotional instability and sexual inversion, claimed, on her admission to Tara last year, to be subject to fleeting losses of consciousness which, supported by EEG changes, were diagnosed as being due to petit mal, though the abnormal waves were not of the petit mal pattern. She was therefore placed on anti-convulsant medication, and within a period of a few weeks she became psychotic and had to be certified. It is probable of course, that there was more than one factor involved in the precipitation of the psychosis, but I think that the anti-convulsant treatment cannot be excused. In treating epileptics in a mental hospital it is not an uncommon experience that in pushing the suppressive treatment of fits one not infrequently aggravates the epileptic personality traits.

All in all, the therapeutic prospects in an adult case of psychopathic personality are, generally speaking, forlorn; hence the resignation that is implied in the application of this diagnosis to a case. If anything is to be done for the cases of psychopathic personality that abound in a community it has to be done in the adolescent stage, at the latest, and preferably even earlier in life, when disordered behaviour patterns are manifested, even though few would care to diagnose them at that stage, as indicative of psychopathic personality, for reasons outlined at the commencement of the paper. The hopelessness of therapy is, fortunately, counterbalanced by the relief that the years bring. As middle age steals upon the psychopath, robbing him, in common with others of his age, of the passionate urges and the unreasoning and unrelenting drives of the younger years, he is better able to accept

the restrictions of society and circumstance. But he has not been won over to conformity, only beaten into non-defiance; not by man. The family and the community can better cope with the psychopath of advancing years, but he is still the psychopath in disposition, makes little or no contribution to their weal and wealth, and usually creates the problem how he can best be accommodated and supported.

SUMMARY

Psychopathic personality is distinguished from psychoneurosis by the comparative absence of conflict and anxiety, and from psychosis by the absence of psychotic features, except during the brief episodic disturbances which characterize the condition. During such passing interludes the presentation may well be of a psychotic nature.

Psychopathic personality is essentially a behaviour and character disorder. It may follow brain disease or injury, but the diagnosis is generally applied to cases which have no apparent cause. The aetiology is regarded as being partly genetic and partly due to early abnormal environmental influences. In not a few cases the condition is associated with some manifestation of epilepsy. There is relative absence of insight and capacity for transference in these cases, and they therefore prove resistant to psychotherapy.

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FURTHER STUDIES ON DIETARY FAT AND THE SERUM CHOLESTEROL

RESEARCH FORUM, UNIVERSITY OF CAPE TOWN

At a meeting of the Research Forum, University of Cape Town, held at the Groote Schuur Hospital, Cape Town, on 5 June 1957 a paper on *Further Studies on Dietary Fat and the Serum Cholesterol*, was presented by Drs. H. Gordon and B. Lewis and Professors L. Eales and J. F. Brock, of the Department of Medicine, University of Cape Town, and Groote Schuur Hospital, Cape Town (C.S.I.R. U.C.T. Clinical Nutrition Research Unit). The following is an abstract of the paper:

A study of the factors modifying the serum-cholesterol level is of general biological interest and may have considerable practical importance. In 1955, in this Forum, Dr. Bronte-Stewart described the initial investigations of our research group into the effect of different dietary fats on the serum cholesterol. It was shown that, in acute experiments, some unsaturated fats (oils) of vegetable and marine origin lower the serum-cholesterol level. Similar observations have been made by workers in several parts of the world. We have extended these early studies and this communication is presented as an interim progress report.

1. Can the cholesterol-lowering effect be maintained or is this effect just a transient metabolic response to an acute dietary change?

In 2 Bantu men, in the controlled environment of a metabolism ward, sunflower-seed oil and cottonseed oil have maintained low serum-cholesterol levels for 2 months. In both men, saturated fat produced prompt and substantial increases in the serum cholesterol. A number of European men (normal and coronary cases) are being studied as out-patients; they maintain their normal activity and consume free but roughly constant diets. After control periods of up to 3 months, a fat supplement (usually 50 g. of sunflower-seed oil daily) is given for about 6 months.

A further control period follows. The subjects' weights and serum-cholesterol levels are recorded at approximately weekly intervals. Studies have so far been completed on 7 men, in 6 of whom a mean reduction in the serum-cholesterol level of 36 mg. % has been maintained during the 6 months on the oil. On stopping the oil, the cholesterol level returns to about its control level. In the 7th subject, the sunflower-seed oil supplement produced no change in the serum cholesterol.

2. What is the effect of feeding an unsaturated fat with a saturated fat?

In 3 men in the metabolism ward, a marked increase in the serum cholesterol was produced by adding 75 g. of hydrogenated coconut fat to their low-fat diet. The further addition of 75 g. of sunflower-seed oil to the diet for 20 days lowered the serum cholesterol but the basal level was not regained. In a 4th subject, 100 g. of hydrogenated coconut fat maintained a raised serum-cholesterol level for about 2 months; the addition of 100 g. of sunflower-seed oil, brought his serum cholesterol down to below basal level, where it remained for a month. When the sunflower-seed oil was stopped, the serum cholesterol returned to its former high level.

3. What effect has cooking on the action of sunflower-seed oil?

Heating the oil in an open aluminium pot for 2 hours did not materially affect its lowering action on the serum-cholesterol level, when compared with the raw oil.

4. Is sunflower-seed oil normally absorbed when fed in large quantities?

Studies in 7 subjects revealed normal absorption of sunflower-seed oil and hydrogenated coconut fat when consumed separately

100 g. of either) or together (75 g. of each) for 10-20 days. Another subject, however, produced fatty stools when fed with 100 g. of sunflower-seed oil, although he absorbed 100 g. of hydrogenated coconut fat normally. This case is exceptional, and in the other subjects relative malabsorption of sunflower-seed oil was not responsible for its cholesterol-lowering effect.

5. How does sunflower-seed oil exert its effect on the serum cholesterol?

In attempting to answer this question, we have begun by examining the faecal excretory products of cholesterol, i.e. the neutral sterols and the bile acids. For the neutral sterols we have only measured the Liebermann-Burchard reacting fraction.

The faecal bile acids were measured by a method devised by one of us (B.L.). Observations were made on 7 subjects, who were fed with sunflower-seed oil before, in addition to, or after hydrogenated coconut fat. Slightly more neutral sterol was excreted when sunflower-seed oil was given; this may partly reflect the greater amount of these sterols in sunflower-seed oil (751 mg.%) than in hydrogenated coconut fat (303 mg.%). In 6 of the 7 subjects bile acid excretion was approximately doubled when sunflower-seed oil was fed. This suggests the possibility that in exerting its effect on the serum cholesterol, sunflower-seed oil promotes the catabolism of this sterol and its excretion from the body.

POLIOMYELITIS VACCINE REGULATIONS

The Minister of Health, after consultation with the South African Medical and Dental Council, has amended the Therapeutic Substances Regulations made under section 83 of the Medical, Dental and Pharmacy Act 1918 by the addition of the following new regulations as Part 1 (D) of the Second Schedule (Government Notice 759 of 24 May 1957):

PROVISIONS APPLICABLE TO VIRAL VACCINES INACTIVATED POLIOMYELITIS VACCINE

Definition and Proper Name

1. This Schedule applies to any inactivated vaccine prepared from poliomyelitis virus.

The proper name of any such vaccine is 'Poliomyelitis Vaccine'.

Strains of Poliomyelitis Virus

2. The strains of poliomyelitis virus used for the preparation of poliomyelitis vaccine shall be only such as have been approved by the licensing authority.

Staff of the Establishment

3. The establishment in which poliomyelitis vaccine is prepared and tested, as prescribed by this part of this Schedule, shall be under the complete direction and control of a person who in the opinion of the licensing authority is regarded as an expert in virology.

Production Records

4. (i) The licensee shall—

(a) keep full protocols in a form approved by the licensing authority on the preparation and testing of each and every batch of vaccine on which he has commenced manufacture; and
(b) forward these completed protocols to the licensing authority in respect to each batch of vaccine on which he has completed manufacture and for which he desires a certificate of release as provided for in section 14 of this part of this Schedule.

(ii) The licensee shall also, if required so to do by the licensing authority, forward as soon as is reasonably possible, to the latter—
(a) the completed protocols in respect of every batch of vaccine on which he has completed manufacture whether the batch passes or fails any of the tests prescribed in this Schedule and whether or not he desires a certificate of release; or

(b) these protocols, completed as far as is possible, in respect to every batch of vaccine on which he has commenced but abandoned manufacture and he shall state therein his reasons for such abandonment.

Provisions as to the Tissue for the Production of Poliomyelitis Virus

5. (i) The tissue used for the production of poliomyelitis virus shall be the kidney tissue of healthy monkeys of a species which has been approved by the licensing authority for this purpose.

(ii) The kidney of a monkey shall not be used for this purpose—
(a) unless the monkey has reacted negatively to a tuberculin test carried out in a manner approved by the licensing authority during the preceding two weeks; or

(b) if the monkey has been previously used for any experimental purpose; or

(c) if on post-mortem examination undertaken under the supervision of a competent medical practitioner or veterinarian any significant gross pathological lesions is revealed; provided that—

If the only experimental purpose for which the monkey has been used is the tests prescribed by section 11 or 12 of this part of this Schedule, its kidneys may be used if, since the beginning of the tests, it has shown no clinical abnormality.

Method of Producing Virus Suspensions

6. (i) Poliomyelitis virus for preparing monovalent type lots for the vaccine shall be grown with aseptic techniques in tissue cultures containing—

(a) a suitable nutrient fluid;
(b) viable cells, trypsinised or non-trypsinised, from the kidneys of monkeys;
(c) suitable antibiotics in the smallest effective concentration as approved by the licensing authority; and
(d) if the licensee desires, phenol red in a concentration not exceeding 0.002 per cent.

(ii) No extraneous protein which is capable of producing allergic effect on injection into human subjects (such as embryonic extracts which have not been subjected to ultrafiltration, and animal serum) shall be added to the tissue cultures prepared as aforesaid, and if animal serum is used at any stage in the manufacture, it shall not be issued in such quantity that the final medium shall contain more than one part of animal serum in one million.

(iii) The virus suspension of the monovalent type lots shall be filtered at suitable intervals by a method approved by the licensing authority.

(iv) The total volume of any monovalent type lot suspensions prepared at any one time shall not exceed a volume which has been approved by the licensing authority as the maximum total volume allowed for such a suspension.

Tests of Virus Monovalent Type Suspension

7. (i) After filtration each monovalent type lot suspension shall be tested by a method approved by the licensing authority to determine the minimum infective dose for a tissue culture, and it shall not be used in the next stage of the preparation of poliomyelitis vaccine unless it contains at least one million such doses per millilitre.

(ii) The suspension shall also be tested by methods approved by the licensing authority for the presence of B virus and of Myco-bacterium tuberculosis.

(iii) When a suspension is considered ready for testing to determine whether the strain of virus which it contains is attenuated, the suspension shall be tested for attenuation by a method approved by the licensing authority.

Method of Inactivating Virus Suspensions

8. (i) All virus infectivity in the virus monovalent type lot suspension shall be destroyed by a method employing formaldehyde or some other means and as approved by the licensing authority.

(ii) The course of the inactivation procedure shall be checked from time to time by methods approved by the licensing authority.

and the minimum period of inactivation shall be estimated from the results of these checks.

Tests for Inactivation

9. (i) When the minimum period of inactivation has been estimated in relationship to a monovalent type lot suspension, a sample of not less than 500 millilitres of the suspension shall be withdrawn by a suitable method three days before the end of that period and a further similar sample shall be withdrawn at the end of that period. Each sample shall be tested by a method approved by the licensing authority for the presence of active virus.

(ii) The suspension shall be regarded as inactivated if neither sample is shown to contain active virus. If the sample withdrawn at the end of the period of inactivation does not, but the sample withdrawn three days before the end of that period does, contain active virus, the suspension may be subjected to inactivation in accordance with the last preceding paragraph for a further three days. The suspension shall then be regarded as inactivated if, at the end of that period a further sample of not less than 500 millilitres, withdrawn and tested in the same way as the other samples, contains no active virus.

Preparation of Vaccine

10. (i) Poliomyelitis vaccine shall be made by mixing the inactivated monovalent type lot suspension of poliomyelitis virus of types 1, 2 and 3, in such proportions as have been approved by the licensing authority, to make a trivalent pool.

(ii) Samples of each such trivalent pool shall be withdrawn and tested in accordance with sections 11 and 12 of this part of the Schedule before the filling of the final containers and before the addition of a bacteriostatic. If the licensing authority so requires, portions of these samples shall be made available to the licensing authority.

Tests for the Safety of the Vaccine

11. (i) A sample of at least 1,500 millilitres of each trivalent pool shall be tested by methods approved by the licensing authority for the presence of active virus.

(ii) Each trivalent pool shall also be tested for the presence of active virus by inoculation into monkeys and the species of monkey and minimum number of monkeys to be used on the test and the methods of the tests to be employed shall be such as have been approved by the licensing authority.

(iii) Each trivalent pool shall also be tested for the presence of L.C.M. virus by a method approved by the licensing authority.

(iv) Vaccine from any trivalent pool shall not be issued for use in human beings if it fails to pass any of the tests prescribed by this section.

Tests for Antigenicity of Vaccine

12. Each trivalent pool shall be tested in a suitable species of animals for its power of producing antibodies to all three types of poliomyelitis virus and the species of animals to be used in these tests and the methods of carrying them out shall be such as have been approved by the licensing authority.

Certificate of Licensing Authority for Release of Vaccine for Issue

13. The licensee shall not issue any batch of poliomyelitis vaccine for use in human beings unless it has been certified by the licensing authority to have satisfactorily passed all the tests prescribed in this part of this Schedule.

14. The licensee shall not, except in a manner which has been approved by the licensing authority, dispose of any batch of poliomyelitis vaccine, or portion thereof—

(a) which has been manufactured in or imported into the Union of South Africa and which has not been granted a certificate of release as provided for under section 13 of this part of this Schedule; or

(b) on which manufacture in the Union of South Africa has been commenced but abandoned.

Bacteriostatic

15. If poliomyelitis vaccine is issued in multidose containers, a bacteriostatic shall be added and its nature and the concentration in which it is used shall be such as has been approved by the licensing authority.

Labelling

16. The label on the container of poliomyelitis vaccine shall state—

- (i) the date after which the preparation may not be used;
- (ii) the precautions necessary for preserving the properties of the contents until that date;
- (iii) the nature of any bacteriostatic added; and
- (iv) the proper dose for administration of the injection into a human subject.

Method of Issue

17. Poliomyelitis vaccine shall not be issued for use in human beings with any other material without the consent of the licensing authority.

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B.C.G. VACCINE : MINISTER'S STATEMENT IN PARLIAMENT

BY OUR PARLIAMENTARY CORRESPONDENT

The immunization campaign against tuberculosis with B.C.G. vaccine has not been abandoned, according to an announcement made by the Minister of Health, Mr. J. H. Viljoen, in the House of Assembly.

The announcement was made by way of a reply to Mr. A. Hepple (Rosettenville) who wanted to know what were the reasons for the abandonment of the proposed immunization campaign with B.C.G. vaccine, and the consequent closing down of the B.C.G. laboratory, referred to in the report of the South African Institute for Medical Research for 1955.

The Minister said that the B.C.G. laboratory of the South African Institute for Medical Research was closed down because of difficulties experienced in connection with the manufacture of B.C.G. vaccine, supplies of which could be obtained regularly from the Serum Institute in Denmark.

Since then 'freeze-dried' vaccine, which was suitable for use in South Africa, had been developed overseas and arrangements were being made by the Department of Health for the importation of supplies of this vaccine.

POLIOMYELITIS VACCINE PRODUCED IN SOUTH AFRICA

STATEMENT IN PARLIAMENT BY THE MINISTER OF HEALTH

BY OUR PARLIAMENTARY CORRESPONDENT

The Polio Research Foundation had informed him that in future its normal production of poliomyelitis vaccine would be two million doses per annum, said the Minister of Health, Mr. J. H. Viljoen, when he replied to points raised in the debate on the Health Vote in committee of supply in the House of Assembly. As far as the present position was concerned, the Foundation had so far received 583,000 applications for polio vaccine, 646,000 doses had already been issued, and the final consignment of 50,000 doses of the 300,000 which had been imported from America, was now being issued.

It could therefore be taken for granted that all children on whose behalf application had been made for the vaccine had already received the first inoculation and that approximately one million doses were still required for the second and third inoculations. The age groups which had been inoculated so far were 3-6 years.

Mr. Viljoen said the Foundation had informed him that more than 600,000 doses would be ready before the end of the year and that an additional 800,000 would be available between September and December this year. Furthermore, 1,080,000 doses which had already been manufactured were at present undergoing safety and efficacy tests. Under the circumstances, the Foundation would soon be in a position to meet the country's immediate polio vaccine requirements and when production was stepped up to two million doses a year, the Foundation would not only be able to satisfy the normal demand, but also build up a reserve to meet any unforeseen contingency.

The Government were not yet prepared to introduce compulsory immunization against polio, but had always encouraged the public by means of radio talks and newspaper articles to ask for the vaccine. It would be a 'terrible' responsibility for any Government to accept a policy of compulsory immunization. It had been more or less possible to determine the efficiency of the vaccine produced in South Africa. 'We are satisfied that the result has been very favourable,' said the Minister.

'It must be remembered that although we have had this success with our polio vaccine, it is something new which is being applied in South Africa, and I want to pay tribute to those research workers like Dr. Gear and others who have succeeded in giving us this vaccine with such effectiveness and speed.'

The Minister said there was no restriction preventing doctors and chemists from importing vaccine from overseas if they preferred it to the locally manufactured article.

DIVIDED CONTROL

Replying to points raised by a former Minister of Health, Dr. H. Gluckman, the Minister agreed that the divided control of health services between the Provinces and the Central Government caused certain difficulties. Bantu health services were receiving the attention of the Department of Health, in collaboration with the Department of Native Affairs and the Provincial authorities, and it was felt that here a real start was possible to find out what re-adjustment could be made to render health services more effective.

Mr. Viljoen agreed with Dr. Gluckman that as the Bantu territories developed, there would have to be better planning. He gave the assurance that he and his department were fully aware of the necessity for planning in advance.

TUBERCULOSIS

Good progress had already been made in regard to tuberculosis. The Department of Health of the Central Government today carried seven-eighths of the costs, whereas in the past the provincial and local authorities had always been responsible for 25-35% of the costs.

The Minister said that never before had the campaign against tuberculosis been carried out at such a great pace as at present.

'As far as the disease among the European population is concerned, we have progressed so far that at Westlake we have been able to evacuate certain wings of a hospital which had been at the disposal of European tuberculosis patients and place them at the disposal of non-European patients for whom there was no accommodation previously.'

'Where 2½ years ago we had 6,200 beds in our hospitals for tuberculosis, we have now succeeded in pushing the number up to 15,000 beds.'

INFLUENZA

The Minister said that the health authorities in the various Union ports had been given strict instructions to ensure that nobody

was allowed to land from ships which had passengers on board suffering from Asiatic influenza. So far, the Union had not had a single case of this disease.

"In the meantime our research services are already investigating the virus which causes the disease and are trying to effect measures to fight it should we have an unexpected outbreak. We do not know whether it is transmitted by contact between people, or whether it is spread through the air. But such steps as can be taken to be prepared for the disease, have already been taken."

Replying to a suggestion by Mrs. S. M. van Niekerk (Drakensberg) that the medical profession should be asked to report cases of Asiatic influenza, the Minister said this was something which his department might bear in mind.

RADIATION HAZARDS

Two South African doctors who had received Fellowships from the World Health Organization, are at present overseas where they are making a special study of the dangers of radiation. The Minister said that when these two doctors returned to the Union, they would be equipped with knowledge concerning the necessary precautions against the dangers of radiation.

Steps had already been taken in connection with radiation given off by equipment used in hospitals. However, he would give renewed instructions to his department to see what further investigations could be made and what other precautions could be taken against the radiation given off by X-ray and other equipment.

LEPROSY

Speaking of leper colonies, Mr. Viljoen said he was advised by a Standing Committee comprising the Secretary for Health, Dr. du Pré le Roux and a number of prominent medical men.

At a meeting held on 19 October 1956 the committee considered the question whether there should not be a change in the policy of compulsory isolation of lepers, and came to the following conclusion:

"Leprosy, which at one stage threatened to become a serious national health problem in the Union, was efficiently controlled by the sympathetic application of the laws regarding compulsory isolation, even before chemotherapy had become available."

The discovery of efficient chemotherapeutic materials and the good results achieved therewith, has given rise to the question whether there should not be a change of policy. After careful consideration of the matter, the committee is of the opinion that, in view of the fact that the disease at present is mostly prevalent among that section of the population which does not realize its infectiousness, it would not be in the interest of the country at this stage to depart from a policy which so far had been so successful."

The committee stated that there were 20 Europeans, 41 Coloureds, 1,218 Natives and 5 Asiatics suffering from leprosy in the Union.

The Minister added that the incidence of leprosy in South Africa was about 37 per 100,000, while in other African territories it was as high as 100 per 100,000.

IN MEMORIAM

MARINUS VAN DEN ENDE, M.B., CH.B. (CAPE TOWN), PH.D. (CANTAB.), F.R.S.S.A.F.

Professor James T. Louw, of Cape Town, writes: Professor Marinus van den Ende, Dean of the Faculty of Medicine and Professor of Bacteriology in the University of Cape Town, died in the Groote Schuur Hospital on 4 June 1957. He was 45 years old.

Having received his schooling in Potgietersrust, he became an undergraduate student in the University of Cape Town, where he qualified in December 1933 having gained distinction in Anatomy, Physiology, Pharmacology, Bacteriology, Psychiatry and Surgery. In 1935 he became Junior Assistant in the Department of Pathology at Cape Town, and in 1937 he was appointed the second John Lucas Walker student in the Department of Pathology, University of Cambridge, which University conferred the degree of Ph.D. upon him in 1939. From then onwards he worked as a member of the scientific staff of the Medical Research Council. His main investigations centred upon the spread of infection through air, and its prevention. It was here he met and became an intimate friend of Sir Henry Dale. Dale's forcefulness, clear insight and absolute

academic honesty had an immense effect upon van den Ende. In 1943 he was seconded from the National Institute to the R.A.M.C. as a major in order to undertake chemotherapeutic and other studies in relation to certain virus and rickettsial diseases in the North African and Italian war zones. In January 1945 he was seconded to the Wellcome Foundation to direct the

large-scale manufacture of scrub typhus vaccine. This included the designing and equipment of laboratories, the preparation of the vaccine, and research into scrub typhus.

February 1946 saw van den Ende appointed to the Chair of Bacteriology in the University of Cape Town. He immediately embarked on a complete renovation of that department and undertook an immense volume of research work—always with the emphasis on virology. He soon isolated a virus which was thought to be responsible for lumpy skin disease in cows. Recognizing his ability and his phenomenal energy and powers of concentration, the C.S.I.R. established a virus research unit in the University of Cape Town. That great philanthropist, Sir Arthur Sims, met him and immediately decided that much could be gained if van den Ende could meet Sir Macfarlane Burnett and work with him for a time. Finances were arranged and in January 1953 Professor and Mrs. van den Ende left for Australia, where he worked in the Walter and Eliza Hall Institute of Medical Research, Melbourne. Whilst he was in Australia his colleagues and our late principal, Dr. T. B. Davie, realizing his immense ability, chose him as the Dean of the Faculty of Medicine.

It was during the closing stages of his Australian visit that he took grievously ill—with an illness that would have broken a lesser man. He accepted his fate and, despite never being in good health, took on the Deanship, became the University's representative to the South African Medical and Dental Council, was elected F.R.S.S.A.F., was appointed as a member of the Government's Commission of Enquiry into Medical Research for South Africa, was appointed a member of the Government's Expert Advisory Committee on Poliomyelitis, and took on work as member of a host of committees in the University. The Senate chose him as one of their Members to the University Council. He became a member of the South African Council for Scientific and Industrial Research. For several years he has been an 'Adviser' to the World Health Organization in influenza. Amongst these multitudinous duties he still found time to be a member of the Rondebosch Boys' High School Committee and in 1957 the University of Cape Town Rugby Football Club honoured him by electing him their President. It must be emphasized that when he took on membership of any committee he immediately became an active member, not sparing himself from sub-committee work. His 'home-work' was always thoroughly done.



Dr. M. van den Ende
Photo Chas. Field, Wynberg

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In fact, he almost invariably found himself chairman of the committee on which he was serving. In March 1956 he was 'one of the few' chosen experts in the world invited to London to take part in a symposium on virology.

In October 1956 the South African Medical Association did him the singular honour of bestowing upon him its first silver medal for 'exceptional original research and valuable contributions to the advancement of medical science and the art of healing.'

Marinus van den Ende was an exceptional man in every respect. Some would classify him as a genius. He was an exceptionally clear thinking, upright and honest man. He was a prodigious worker, with a flair for analysing a problem, breaking it down to its basic facts and then constructing reasonable, correct and useful conclusions. As a friend there could be none better. He was most considerate and kind, ever on the alert for the possibility of lending a helping hand. He spoke ill of no man. As a human being, as a professor, as a dean, he set an outstanding example to the students, his friends and his colleagues. He had no foes

because he dealt with human beings as he dealt with all problems—he got to the pith of the matter and won opposition over to his way of thinking by sound argument.

The University of Cape Town has been struck heavy blows in rapid succession. It can ill afford to lose giants like Davie and van den Ende at this crucial moment. It may rock but it will remain steadfast because it has been built on sound foundations. Memories of deeds done by these men, the way in which these deeds were wrought, the bravery and devotion to duty shown by them whilst mortally ill, are further cornerstones of rich tradition.

Marinus van den Ende's life was one of absolute devotion to high duty. The standard set by him, his vision and the attention he paid to important detail, together with the fineness of his character, will leave its hallmark on the Medical School, the University and all those who have been fortunate enough to be associated with him. To his widow, his two sons and his two daughters a deep and heartfelt sympathy is extended in their irreparable loss.

PARKING BY DOCTORS IN CENTRAL CAPE TOWN

The Cape Town City Council has passed new traffic regulations dealing with the parking of motor vehicles in the 'central area' of Cape Town by medical practitioners. This is in the nature of a 'first reading'. The draft regulations, having been published, will again come before the City Council for confirmation, and will then be subject to approval by the Administrator of the Cape Province. Only then will they come into operation.

The 'central area' is defined as an area in Cape Town bounded by the following thoroughfares: Roeland Street, Stal Plein, Parliament Street, Bureau Street, Adderley Street, Wale Street, Queen Victoria Street, Grey's Pass, Orange Street, Overbeek Square, Long Street, Dock Road, Adderley Street, Castle Street, Buitenkant Street.

The regulations authorize the Council's Licensing Officer, on application, to issue a token to any medical practitioner who, in carrying out his professional duties, regularly attends any consulting room, clinic, hospital, nursing home or health department in the 'central area'. The token, which bears a white cross on a black circular background 2 inches in diameter, is to be affixed to the practitioner's motor vehicle so as to be visible on the near side from in front. A fee not exceeding £1 is payable for the token.

In respect of any motor vehicle to which the token is affixed the medical practitioner is exempted from the provisions of

section 87 (1) (a) of the Road Traffic Ordinance 19 of 1955 in so far as they apply to the 'central area'; but only from 8 a.m. to 6 p.m., and not in any 'closed street'. (The 'closed streets' are portions of Church, Longmarket, Shortmarket, Hout, Castle, Bureau and Parliament Streets from 8 a.m. to 6 p.m., and portions of Darling, Strand and Adderley Streets during such hours as non-stopping regulations are in force.)

Section 87 (1) (a) of Ordinance 19 prohibits the parking of a vehicle 'in contravention of a road traffic sign in the prescribed form' and the exemption accorded by the draft regulation applies to this prohibition only. For instance, though by reason of the exemption it will not be an offence merely to park in a place not marked as a parking place or a place marked for 'no parking', or for a period exceeding the prescribed time, yet the exemption will not apply to other offences, such as parking within 15 feet of an intersection or 20 feet of a fire hydrant, or 'double parking', or parking too far from the curb, or across a vehicular side-entrance to a public road, or at bus stops or no-stopping areas or off-loading areas, etc.; nor will the exemption apply after 6 p.m. or outside the 'central area'.

The Licensing Officer will not only have the right to refuse to issue a token, but also to withdraw one already issued. An appeal against either action may be made to the City Council.

PASSING EVENTS : IN DIE VERBYGAAN

The British Medical Association notifies for information that the title of the Empire Medical Advisory Bureau has been changed to 'Commonwealth Medical Advisory Bureau' and the title of the International Medical Visitors Bureau to 'International Medical Advisory Bureau'.

* * *

Public Health, the Journal of the (British) Society of Medical Officers of Health, has been published in London by the Society of Medical Officers of Health for the past 71 years, and is well recognized as an authoritative journal in the field of preventive medicine. As part of a scheme of reorganization of the Society's administration it has been decided to separate the management of the journal from the secretarial work of the Society, and the publication of *Public Health* has now been entrusted to Baillière, Tindall and Cox Ltd., 7 and 8 Henrietta Street, London, W.C. 2. The Society, however, will retain full editorial control, which will continue to be exercised by an elected Editorial Board, and *Public Health* will continue to be the official organ of the Society.

The first issue of the Journal under the new management appeared in April 1957 as Volume 71, No. 1. The format has been entirely changed to bring it into line with modern ideas.

The April number consists of 40 pages of matter, and comprises 3 signed articles by English medical officers of health and also editorial articles, book reviews and Society news. The annual subscription is 42s., post free; single copies 4s., post free.

* * *

Archives of Physical Medicine and Rehabilitation. The Editorial Board of this Journal, which is the official journal of the American Congress of Physical Medicine and Rehabilitation and the American Academy of Physical Medicine and Rehabilitation, have established a special subscription rate of \$5.00 per year to be granted to bona fide residents in physical medicine and other specialities in certain countries, including the Union of South Africa. The following rules apply: (1) The subscription may be entered for a period not to exceed 3 years. (2) All orders must be accompanied by a letter of verification from the director of the training programme confirming the resident's status and the number of years remaining in the resident's training programme. (3) This special rate is not applicable if less than one year of training remains to be completed in the applicant's residency programme. (4) The subscription is not transferable and must be entered in the resident's name. It cannot be sent to a hospital, organization or institution, or to a person other than the sub-

scriber. Applicants should write to: The Archives of Physical Medicine and Rehabilitation, 30 N. Michigan Avenue, Chicago 2, Illinois, U.S.A.

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Mr. W. T. Ross, F.R.C.S., of Johannesburg has been elected a Fellow of the British Orthopaedic Association

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South African Society of Medical Women. The annual general meeting of the Cape Town Sub-group of this Society will be held in the Cafeteria, Medical Students' Residence, Mowbray, Cape, on Wednesday 26 June at 6.45 p.m. Supper will be served, and in addition to the business meeting, Dr. J. van der Horst and Dr. I. Robertson will describe the conferences they attended in Madagascar and Switzerland respectively. Will all members intending to be present please telephone or write to Dr. O. John-

ston, 'Silverleaves', Rhodes Drive, Constantia, telephone 7-7156 before 24 June. Medical women wishing to join the Group are welcome to attend.

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Union of South Africa. Department of Health. Notification of formidable epidemic diseases and poliomyelitis in the Union during the period 22 May-28 May 1957.

	Eur.	Nat.	Col.	Asiat.	Total
Transvaal ..	2	2	—	—	4
Cape Province ..	2	4	13	—	19
Orange Free State ..	2	1	—	—	3
Natal ..	2	1	—	1	4
Totals ..	8	8	13	1	30

Plague, Smallpox, Typhus Fever: Nil.

NEW PREPARATIONS AND APPLIANCES : NUWE PREPAREAT EN TOESTELLE

'Furadantin'—A Broad-Spectrum Nitrofuran for Urinary Infections

SKF Laboratories (Pty.) Ltd. announce that from June they will be manufacturing and distributing 'Furadantin', and supply the following information for the treatment of refractory urinary infections. 'Furadantin' (nitrofurantoin) is effective against the majority of urinary pathogens including *Proteus* and some *Pseudomonas* infections. It is truly broad-spectrum in its antibacterial action, yet it does not hinder future medication with antibiotics or sulphonamides since it is unrelated to them. Cross resistance is unknown.

Therapeutic action is rapid—effective concentrations are present within 30 minutes of ingestion and most patients are asymptomatic and the urine free from pus cells within 3 days, while the urine is usually sterile in 1 week.

'Furadantin' is safe to prescribe and can be useful in the treatment of children and pregnant women. There is virtually no risk of crystalluria.

Side-effects are mild and the occasional case of nausea can be controlled by taking the tablets with a meal. The usual adult

dose is 2 tablets q.i.d., at mealtimes and on retiring. 'Furadantin' is available in containers of 25 tablets, each tablet containing 50 mg. of nitrofurantoin. Further details and samples may be obtained from: SKF Laboratories (Pty.) Ltd., P.O. Box 784, Port Elizabeth.

* * *

New 'Elastoplast' Airstrip. Smith & Nephew (Pty.) Ltd., of Pinetown, Natal, announce the introduction of a new type of first-aid dressing for minor cuts and wounds. Called Elastoplast Airstrip, these adhesive dressings are made from a micro-porous base material which allows wounds to breathe yet keeps them fully waterproof. Thus, wounds heal faster under ideal conditions, with no maceration however long the dressing is kept on. Elastoplast Airstrip is available in boxes containing assorted sizes for 1s. 6d. and 3s. and also in professional packs.

Further information from: Mr. H. S. Buckley, Messrs. Smith & Nephew (Pty.) Ltd., Gillitts Road, Pinetown, Natal. Telephone: 76671 Durban.

REVIEWS OF BOOKS : BOEKRESENSIES

MINIMAL PULMONARY TUBERCULOSIS

Minimal Pulmonary Tuberculosis Found By Mass Radiography (Fluorography). A Report to the Prophit Committee by V. H. Springett, M.D., M.R.C.P., and including results of work done by A. J. Eley, M.A., M.B., B.S., D.M.R.(D.). Pp. xiv + 233. LXV Plates. Illustrations 16 line in text. £2 2s. net. London: H. K. Lewis & Co. Ltd. 1956.

Contents: A. Methods and Criteria. B. Yield of Minimal Lesions. C. The Initial Radiograph. D. Background of Patients Examined. E. First Clinical Examinations. F. Bacteriology. G. Duration of Survey Observation. H. Clinical Observations within Five Years. I. Radiographic Changes within Five Years. J. Results of Bacteriological Examinations within Five Years. K. Clinical Tests During Five Years Observation. L. Relationships between Clinical, Radiographic and Bacteriological Results. M. Results of First Examination Related to Radiographic and Bacteriological Results in Five Years. N. Further Details of Certain Groups. O. Treatment Related to Clinical Radiographic and Bacteriological Results. P. Treatment. Q. Status at Various Intervals and Mortality. R. General Summary and Comparison with Results of other Surveys. S. Management of Minimal Tuberculosis. Appendices. Tables. References.

Early diagnosis in the treatment of pulmonary tuberculosis has always been recognized as being of the utmost importance. This volume deals with 1,213 cases of minimal pulmonary tuberculosis discovered by two mass radiography units in London during the years 1946 to 1948. Of the total number of cases in the survey, 269 were found to be sputum-positive. A follow-up was made over a period of 5 years and the records were analysed. The treatment of all the cases was under the control of the local chest physicians and private practitioners who used rest, artificial pneumothorax, pneumoperitoneum and phenric crush as the main forms of treatment since streptomycin and PAS were not readily obtainable, particularly in the earlier years of the survey.

Despite the fact that the treatment given has been largely rendered out of date by the advent of antibacterial therapy, there were only 4 deaths from tuberculosis recorded, which emphasizes the excellent prognosis in early pulmonary tuberculosis provided the patient is kept under observation and given such treatment as may be necessary.

This book should prove of great interest to all those concerned in the problem of pulmonary tuberculosis, and even practitioners with little free time at their disposal can, as the authors point out, gain an excellent general outline of the work covered by reading certain specified chapters and summaries.

H.L.A.

OBSTETRICS AND GYNAECOLOGY

Year Book of Obstetrics and Gynecology—1956-1957 Series. Edited by J. P. Greenhill, B.S., M.D., F.A.C.S., F.I.C.S. (Honorary). Pp. 592. 82 Figures. \$6.75. Chicago: Year Book Publishers, Inc. 1956.

Contents: Obstetrics. Pregnancy. Labor. Puerperium. The Newborn. Gynecology. General Principles. Diagnosis. Infertility. Operative Technic. Infections. Nonmalignant Neoplasms. Malignant Tumors. Menstrual Disorders. Endocrinology.

After 57 years of publication, this 1956-57 series, edited by Professor Greenhill, maintains its high tradition and interest. Indeed, many who are in busy practice look forward to this most interesting perusal of the recent trends in modern Obstetrics and Gynaecology. Of course, the 'Year Book Quiz', which accompanies every publication, is now a routine feature. It is to be wondered how many

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questions could be 'correctly' answered by those of us well up in our reading. The toxæmias of pregnancy, uterine haemorrhage in obstetrics, and infection, as usual occupy a prominent position in this résumé, for they contribute largely to maternal mortality, which in the USA is 3·8 times higher in the non-European than in the European.

The newborn child is well represented, the dangers of prematurity being emphasized.

In the gynaecological section infertility is as usual fully reviewed, and more mention is made of tubal plastic operations, with the use of polyethylene catheters. The results, however, although better than previously, are still not entirely satisfactory.

Some effects in Japan of the Nagasaki atomic bomb are mentioned as causing increased numbers of abortions and stillbirths. Microcephaly due to radiation is now being more fully recognized.

Malignant disease occupies 1/5th of this Year Book, and stress is being laid on vaginal cytological techniques in its diagnosis. Malignant ovarian tumours still kill a large number of women.

It would be impossible to mention all subjects of interest in this book, but it should be the business of every practising gynaecologist to order his copy of the Year Book in order to maintain his knowledge of the most modern trends in this subject.

L.R.

THYMUS TUMOURS

Tumours of the Thymus Gland. By Benjamin Castleman, M.D. Pp. 82. Figures 81. Colour Plates 4. \$1.00. Washington: Armed Forces Institute of Pathology. 1955.

Contents: Introduction. Thymoma. Tumors Resembling Thymoma. Other Tumors of the Thymus Gland.

The study of the thymus gland has always been of absorbing interest, not only because its histology and the changes it undergoes during life are fascinating, but because of the many contradictory and controversial views regarding its function.

Today, although the complicated embryological development of the thymus is well understood, very little more is known of its function. This monograph provides an extremely good atlas of the pathology of thymic tumours, with excellent photographs (black-and-white and in colour). The photomicrographs, some of them in colour, ensure a very clear picture of the disease processes. The monograph is divided into 4 sub-groups. The introduction deals with the normal thymus, and thymic hyperplasia, particularly in connection with myasthenia gravis. Secondly, thymomas are discussed with emphasis on their relationship to myasthenia gravis and Cushing's syndrome, and consideration is given to the malignancy of these tumors.

The 3rd sub-group deals with tumours resembling thymomas, and the final section describes the rarer tumours of the thymus gland.

This excellent monograph should be well received by all general surgeons and physicians, particularly those engaged in the teaching of students.

W.L.P.

ORTHOPAEDIC AND TRAUMATIC SURGERY

1955-1956 Series—*Year Book of Orthopaedics and Traumatic Surgery.* Edited by Edward L. Compere, M.D., F.A.C.S., F.I.C.S. Pp. 333, 211 Figures. \$6.50 Post Paid. Chicago: Year Book Publishers, Inc. 1956.

Contents: Introduction. Anatomy, Embryology, Physiology and Pathology. Congenital Deformities. The Epiphyses. Poliomyelitis. Osteomyelitis and other Infections. Tumors, Cysts and Fibrodyplasia. Arthritis and Rheumatism. Fractures and Dislocations. The Spine and Pelvis. The Neck, Shoulder and Arm. The Hand and Wrist. The Hip, Leg and Knee. Amputations and Prostheses. Surgical and Diagnostic Techniques. Instruments, Appliances and Bone Banks. Calcium and Phosphorus Metabolic Diseases of Bones. Miscellaneous.

Once again, Mr. Compere has produced an excellent résumé of the literature of Orthopaedic and Traumatic Surgery for the years 1955-56.

There have apparently been no major advances in the field of orthopaedic surgery during these years, but results of previous procedures have appeared in abundance in the literature. Statistics and clinical results have been faithfully recorded in a readable and precise form which obviates the necessity for tedious and repetitive study in most of the sections.

The introduction of the Salk vaccine in the United States has not as yet made any difference to the number of cases of poliomyelitis which become potential patients for orthopaedic surgery. It is a recent introduction which will only later affect the future of orthopaedics.

In considering the book in detail, the Anatomy, Embryology, Physiology and Pathology section, and the section on experimental surgery, are rather more extensive than usual, but the articles collected are pertinent and have been wisely chosen.

The book as usual is excellently produced. The précis of articles are discrete, decisive and succinct. The illustrations and reproductions often appear to be better produced than in the originals. For anybody interested in the subject of orthopaedics, this book is essential, since it avoids the necessity for spending all one's spare time reading the original articles.

The Year Book of Orthopaedics has come to be a great stand-by for orthopaedic surgeons, and once again Dr. Compere is to be congratulated on an excellent production.

T.B.McM.

ANATOMY

An Atlas of Anatomy. Fourth Edition. By J. C. Boileau Grant, M.C., M.B., F.R.C.S. (Edin.). Pp. xii + 554 with 714 illustrations (many in colour) in 634 figs. 120s. net. London: Baillière, Tindall and Cox Ltd. 1956.

Contents: Illustrations. The Upper Limb, Figs. 1-100. The Abdomen, Figs. 101-173. The Perineum and Pelvis, Figs. 174-220. The Lower Limb, Figs. 221-330. The Vertebral Column, Figs. 331-367. The Thorax, Figs. 368-438. The Head and Neck, Figs. 439-619. The Cranial Nerves and the Dermatomes, Figs. 620-634.

This magnificently printed tome of illustrations of regional anatomy has gone into its 4th edition within the short period of 13 years. The plates are large, attractively coloured and clear, with explanatory texts. Throughout the world anatomists have constantly utilized this visual aid, and students, whether undergraduate or postgraduate, have gained tremendously by studying or refreshing their memories from Professor Grant's atlas.

In this edition more than 80 of the illustrations are new, and many of the old ones have been either improved or replaced. Of interest among the new illustrations are the basic diagrams of the arteries of the upper and lower limbs, of the digestive canal, and of the tracheobronchial tree; the subacromial bursa; variations in the capsule of the shoulder joint; the mid-tarsal joints; the female perineum; dissections of the hilus of the lungs from various aspects; stages in the eruption of the teeth; the root of the neck; the triangle of the vertebral artery, the stellate ganglion, the paranasal sinuses and their variations, and the pharynx and parotid gland from behind; cross-sections of the limbs and neck and coronal sections of the orbital and nasal cavities, of the cavernous sinus and of the orbital cavity.

Although the author occasionally makes reference to anomalies, particularly arterial, it is suggested that he may consider noting the extremely common variations of the branches of the subclavian artery in the next edition.

This atlas is highly recommended to medical undergraduates and postgraduate students of human anatomy, and to surgeons, who require visual aids to grasp and memorize the subject.

R.S.

CEREBRAL PALSY

The Infantile Cerebral Palsies. By Irene Collis, W. R. F. Collis, William Dunham, L. T. Hilliard and David Lawson. Foreword by Sir Francis Walshe. Pp. xi + 100. 15s. net. London: William Heinemann—Medical Books Ltd. 1956.

Contents: Foreword. I. Introduction. II. W. J. Little. III. The Forms of Infantile Cerebral Palsy. IV. Diagnosis and Management. V. Generalised Spasticity. VI. Hemiplegia. VII. Variable Rigidity. VIII. Athetoid Cerebral Palsy. IX. Ataxic Cerebral Palsy. X. The Organisation of Cerebral Palsy Services. XI. Conclusion. References. Index.

'Cerebral Palsy' has in recent years become a matter of popular interest and many projects have been initiated by socially con-

scious groups and individuals to treat affected children. However well intentioned this work is, it will be largely a misdirected effort unless certain essential facts are constantly kept in mind. Amongst these are that the anatomical lesion itself is not curable and that the only logical treatment is by adaptation of function of those parts of the brain not destroyed by the lesion. As this is a process of learning on the part of the affected child, a basic requirement is that the intellectual function shall not be affected to such an extent as to interfere with learning processes. Therefore a proper diagnosis of the affected child as a total person, and not only as the possessor of a series of disabilities and deformities, followed by prolonged education directed and controlled by experts thoroughly well versed in the neurophysiology of voluntary movements, are all basic requirements which, unfortunately, are not to be found in some centres.

This small book is written by experts with long personal experience of the problem, who have applied the correct principles of diagnosis and therapy in practice over many years. It is thoroughly recommended as among the best of its kind and might well be read by all who are professionally and personally interested.

S.B.

THE PSYCHIATRIC SOCIAL SERVICE IN HONG KONG

Mental Health and Education in Hong Kong. By K. E. Priestley, M.A. (Oxon.) and Beryl R. Wright, B.Ed. (Sydney). Pp. 97. 7s. 6d. London: Oxford University Press. 1956.

Contents: I. Child Guidance work: the present and future in Hong Kong. II. What is normal and what is abnormal in children and young persons (11-18). III. Emotional conflict in personality development, and the task of the school in resolving difficulties. IV. Factors in Mental Health in Hong Kong. V. Mental Health in the Schoolroom. VI. Mental Health of the Teacher. Discussion. VII. Subsequent Group Discussions: to answer questions, to elaborate points, and to suggest future lines of activity. *Skeleton Reading List.* Index.

This short pamphlet represents a courageous venture—it is a blue print of a psychiatric social service in Hong Kong. There was no psychiatric social service, and Chinese-speaking social workers had to be trained. The emphasis has quite rightly been laid on the young, and the lectures deal chiefly with problems arising in children.

It is a little difficult to know to whom the lectures are addressed; apparently to doctors, teachers and interested laymen, in the hope of arousing enthusiasm for a social service. The lecturers point out they are not at this stage able to say whether there is any great difference between western and Chinese psychiatric problems, but they outline in general the problems as they arise in a western civilization. They stress some of the differences that are to be noted in Hong Kong and point out that the whole colony is in the process of rapid westernization and that a single family may contain atheists, Buddhists and Christians. They draw some attention to the heroin addiction and the opium smoking that is prevalent in the colony, and they point out the prevalence of superstitions, which in South Africa form a common basis for psychiatric problems amongst both Coloured and Native patients.

South Africans will be interested in these lectures because the workers are starting from scratch and are obviously only vaguely aware of what the problems they are going to meet will be. They are quite frank about this, but the two lecturers seem very well read and most open-minded, and it will be of great interest to learn in another five or ten years how they have progressed.

The content of the lectures themselves is really a rapid review, in simple terms, of psychiatric problems as they occur to the school teacher and to the social worker. Obviously no comprehensive survey is possible, but the approach is realistic and enthusiastic, and the book is well worth reading for its stimulating sincerity.

J. MacW. MacG.

CORRESPONDENCE : BRIEWERUBRIEK

THE ASIATIC INFLUENZA EPIDEMIC

To the Editor: The occurrence in the East of an influenza epidemic caused by an immunological variant of Type A virus is causing a certain amount of public concern, even though from all reports received symptoms are not unduly severe and mortality has been low.

The Union Department of Health is taking every possible precaution against the introduction of the infection through sea and airports but it will be appreciated that infection may be introduced into the country in spite of these precautions.

Should this occur steps will have to be taken to limit its spread and this can only be done with the full cooperation of all medical practitioners.

It will therefore be appreciated if an appeal can be made to medical practitioners through the columns of your *Journal*:

1. To report any unusual incidence of influenza to the Local Authority in which the outbreak occurs and/or to the nearest Chief Regional Health Officer of the Department in Cape Town, East London, Durban, Bloemfontein, Johannesburg or Pietersburg; telegraphic address—Health.

2. To confine their patients to bed for at least 2 days after the temperature has become normal with the twofold object of limiting the spread of infection and preventing relapses and secondary infections.

A statement by Dr. J. H. S. Gear, of the South African Institute for Medical Research, Johannesburg, is attached.

J. J. du Pré le Roux
Secretary for Health

Department of Health
P.O. Box 3879
Cape Town
10 June 1957

DR. GEAR'S STATEMENT

From information received from the World Health Organization, it is apparent that a widespread epidemic of influenza is occurring

in the countries of the Far East. This epidemic first became apparent in Hong Kong and since then has spread to Singapore, Manila and Tai-Wan and more recently to India, Thailand and Japan. It is probable that this spread will continue.

The disease presents with pyrexia, severe headache, pains in the limbs and back, coryza and sore throat, and sometimes cough and giddiness. The temperature ranges from 101° to 103° F and lasts about 2 days, followed by 4-5 days' debility. Most cases are mild and there have been few complications. However, several deaths have been ascribed to this infection in most of the affected countries. The post-mortem examination has shown petechial haemorrhages in the lungs with general oedema and patchy consolidation, and frothy fluid in the bronchi and trachea. A few cases of influenzal encephalitis have been reported.

The virus has been identified in complement-fixation tests as belonging to the influenza 'A' group. However, it appears to be a new variant of 'A' differing in several respects from previously isolated strains. For those who are concerned with isolation of the strains of influenza in a laboratory, it will be of interest to note that haemagglutination is strongly inhibited by normal ferret sera but is not inhibited by normal mouse sera. Haemagglutinin is formed only to low titre and filaments are formed in the allantoic fluid chick-embryo cultures. This strain appears to be so different from previous strains that existing vaccines will probably not give protection.

Arrangements have been made to prepare vaccine against this strain and this work is already in hand. However, it should be emphasized that it will be possible to prepare only small amounts of vaccine, which will be used to immunize personnel of hospitals and other essential services before any is available to the general public. In any case it will not be feasible to rely on prophylactic vaccination to protect the population from influenza. Reliance will therefore have to be placed on general measures.

It should be emphasized that so far the illness is relatively mild and in the majority of cases the affected individual is able to resume his normal activities after about one week.

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1. Van die
2. Allen, A
3. Cade, S
4. Becker, R
5. McMullen
74, 618.
6. Driver,
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7. Frank, S
8. Sulzberg

PENSION 5

To the Editor
from Dr. John
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KWAADAARDIGE MELANOOM

Aan die Redakteur: Graag wil ek enkele opmerkings maak na aanleiding van u hoofartikel oor kwaadaardige melanoom.¹

Die bewering dat 3% van huidkancers maligne melanome is, is gelukkig nie juis nie. Dit mag die geval wees met huidkancers wat by patoloë ter seksie kom, of deur chirurgie gesien word. Die meeste huidgewas word in die eerste instansie deur dermatoloë gesien en maligne melanome vorm 'n baie geringe persentasie daarvan—seker minder as 1%.

Met die uitstekende oorsigte en klassifikasie van Allen en Spitz² sal iedereen seker graag saamstem. Hierdie outeurs het ook gewys op die belangrike verskille in oorlewingsduur na primêre eksisie by mans en vrouens, nl. 38·8% by vrouens maar net 18·2% by mans by 337 gevalle. By lokalisasie aan die nek en gesig was die getalle 57·5% en 23·3% respektiewelik. Cade³ het in sy artikel hierdie geslagsfaktor ongelukkig nie in aanmerking geneem by sy indeling van oorlewingsduur nie.

In die uiterst interessante artikel van Cade³ kom enkele bewerings voor waaroor die meeste dermatoloë dit seker nie eens sal wees nie. Iedereen sal saamstem dat daar nie met verdagte melanome gepeuter mag word nie, maar 'n wye eksisie met eventuele huidoorplanting is seer seker nie altyd aangewese nie. Becker⁴ het aangetoon dat ongeveer 40 tot 50% klinies gediagnostiseerde melanome nie histologiese bewys kon word nie. Die meeste foute diagnoses het geblyk pigment nevi, blou nevi, gepigmenteerde epitelome, seborrhiese keratoses of verruca vulgaris te wees. In ooreinstemming hiermee is die bevinding van McMullen en Hubener.⁵

Daar is nog geen bewys gelewer dat 'n proefeksisie metaplasie of metastase in die hand kan werk nie. Cade³ maak in sy artikel van hierdie mening melding. Hy verwerp proefeksisie egter as 'n verkeerde handeling en klassifiseer, myns insiens ten onregte, dit as lapwerk. 'Behoorlike stansbiopsie of totale eksisie, waar dit met primêre hefting moontlik is, sal baie pasiënte onnodige leed spaar en behoed teen mutilerende chirurgiese ingrepe. Hierdie procedure word deur meeste dermatoloë—by wie huidtumore in eerste instansie kom—gevolg.^{4,6,7,8} Sodra die diagnose maligne melanome bevestig is, hoort die pasiënt tuis by 'n radikale chirurg, wie nie sal skroom om 'n wye eksisie+blokreseksie van die regionale limfkliere te doen nie. Allen en Spitz² het ook aangetoon dat by 3·6% van hulle gevalle daar multisentriese primêre gevasse was, met 'n neiging tot grensaktiwiteit aan die rande van die geëksidente gevasse.

Deur bogenoemde outeurs en andere is herhaalde kere gewys op die langsame verloop van sommige melanome, selfs nadat metastase opgetree het. Spontane regressie kan soms optree.

Dit mag hier miskien ook van pas wees om te waarsku teen die gebruik van steroïde by pasiënte met melanome, daar dit die gevasse vinniger laat groei.

F. P. Scott

United-Gebou 314

Bloemfontein

27 Mei 1957

1. Van die Redaksie (1957): S. Afr. T. Geneesk., **31**, 469.
2. Allen, A. C. en Spitz, S. (1954): Arch. Derm. Syph., **69**, 150.
3. Cade, S. (1957): Brit. Med. J., **1**, 119.
4. Becker, S. W. (1954): Arch. Derm. Syph., **69**, 11.
5. McMullen, F. H. en Hubener, L. F. (1956): Arch. Derm., **74**, 618.
6. Driver, J. R. (1954): Arch. Derm. Syph., **69**, 150 (in besprekking).
7. Frank, S. B. (1954): *Ibid.*, **69**, 172.
8. Sulzberger, M. B. (1954): *Ibid.*, **69**, 172 (in besprekking).

PENSION SCHEME VERSUS ENDOWMENT ASSURANCE

To the Editor: In the *Journal* of 11 May you published a letter from Dr. John H. Bam on the above subject, and while I have written personally to Dr. Bam, I feel that an explanation is necessary for those members of the Association who may be equally ignorant on this matter of policy. In this connection I feel that all the facts in regard to the question of pension schemes in relation to the Medical Association of South Africa should be set out.

In response to a number of enquiries some years ago and with particular reference to a scheme which was produced by the Norwich Union Life Insurance Society, the Federal Council considered it and two other schemes which had been set out by the South African Mutual Life Assurance Society and the South African National Life Assurance Company (Sanlam). These three schemes were referred back to the Head Office and Journal Committee for consideration and recommendation to Council. After going through them, the Committee recommended that no scheme of the kind outlined in the memorandum put up by the three companies should be accepted, but that members should be encouraged to take out as much endowment assurance as they could afford.

The reason for this recommendation was that the three schemes proposed were all based essentially on endowment assurance which at maturity would be converted into an annuity, thus giving a pension of a fixed amount as long as the member lived. This annuity as income would be subject to income tax, but the annuity would cease with the member's death. Presumably, unless the member had other assets, his widow and any other dependants might become a charge on the Benevolent Fund of the Association. In the circumstances the Committee felt that endowment assurance would be a better investment for members of the Association, so that the proceeds could be invested in property or in any other form of investment that might suit the member at retiring age.

I would mention at this stage that I was supplied with a copy of the memorandum prepared by the Sub-Committee of the Cape Western Branch, through the good offices of Mr. J. D. Joubert, and the Committee was aware of the work which had been done.

The Head Office and Journal Committee's recommendation and report was accepted by Federal Council, but the subsequent proposal by a Transvaal member that a firm of insurance brokers be appointed brokers to the Association to devise some form of pension scheme, was not accepted.

Some months later the South African Mutual Life Assurance Society produced a scheme of endowment assurance based on policies which would mature annually over a period of 20 years from the age of 65. As these would each be a separate policy on maturity the amount would be considered as capital in so far as the Inland Revenue Department was concerned, and so would not be subject to income tax. Should the member die at any time after the age of 65, all policies which had not yet matured would be paid out for the benefit of his widow or dependants. The Committee considered that this was in accordance with its previous recommendation to Federal Council which had been accepted, and as a result the scheme was recommended to all members of the Association for their consideration.

At this time the Professional Provident Society, which had been working on a scheme similar to some extent to that proposed by the Cape Western Branch Sub-Committee, wrote to this office concerning it. As a result I met members of the Committee of the Society in Johannesburg last November and discussed the whole question with them. I was given confidential details regarding the proposed scheme, but it was made clear that it would depend entirely on Government support and that even if the Cabinet was sympathetic it could not come into effect for at least two years. I pointed out that the policy of the Association was that members should try to cover themselves as fully as possible at the earliest possible date and that if members were asked to defer any decision in favour of the Professional Provident Society's scheme it might mean considerable hardship to the family of any member whose death might shortly take place, particularly as there was no guarantee that the scheme would ever be accepted by the Government.

At the recent meeting of the Federal Council this matter was discussed and I gave a full explanation on the lines mentioned above. This was accepted by Council.

In regard to the fourth paragraph of Dr. Bam's letter, I would advise that the Professional Provident Society is not 'run by doctors themselves' but is managed by a Committee of dentists, doctors, chemists and advocates; the Society having originally been established by a group of dentists.

The fifth paragraph of the letter refers to the Association's relation with the Atlas Assurance Company in regard to public liability insurance (malpraxis insurance), and I would advise that a considerable number of members are still insured with this company. The recent arrangement made between the Association

and the Medical Protection Society of London has resulted in some 300 members joining that Society. The fees payable for cover by both the Atlas Assurance Company and the Medical Protection Society are very similar in amount. Dr. Bam has not mentioned the Medical Protection Society, but he refers to 'another very reputable assurance company which gives all the cover that the Atlas does and for a much smaller premium'. As the Atlas Assurance Company has long-standing agreements with the Association to provide cover which is dependent on close cooperation between the Association and the company and which provides an appeal to the President of the Association, it is difficult to understand how any other company other than the Medical Protection Society can give 'all the cover that the Atlas does.' If Dr. Bam has found something that is unusual and could be of benefit to other members of the Association, surely he should make it known to the Association in order that other members may derive similar benefits to those which he apparently has.

A. H. Tonkin

Secretary, Medical Association of South Africa

Medical House
35 Wale Street
Cape Town
18 May 1957.

PROFESSIONAL PROVIDENT SOCIETY

To the Editor: I am about to leave South Africa for overseas, and in the process of tidying up my affairs I have had to realize my investments in the Professional Provident Society of South Africa. I think it right to bring to the notice of the younger members of the medical profession the facts in brief of a genuine settlement.

I joined the Society late 1951 and in monthly payments had subscribed approximately £350, but the full settlement of the amount due to me was a fine cheque for £426 17s. 11d. In other words, having been covered for sickness benefits throughout this period of 6 years, I not only got my money back, but I got interest with it.

Nagenod

27 May 1957

CONTROL OF THERAPEUTIC SUBSTANCES

To the Editor: I was very interested to read in the *Journal* of 11 May, a series of questions answered by Dr. J. C. E. Mullen.¹ The answers fully clarify the legal position. Although the regulations mentioned by Dr. Mullen are in force, there is nothing to prevent any registered pharmacist from preparing and marketing injections. His labels must comply with regulations but his products are not tested by any authority unless they fall under the Therapeutic Substances Regulations.

The person who put the question might perhaps like answers of a technical nature. Saphar Laboratories Ltd. are manufacturers of intravenous solutions and a great deal of work, thought and time is devoted to the control of raw materials and production of the finished preparations. In reply to the questions I should like to outline briefly the control system employed at Saphar Laboratories.

Question 2. Testing of the purity of ingredients

All raw materials are assayed for identity and purity before use. When a substance is received packed in several containers, samples from each container are tested. The following example illustrates the necessity of this. Some time ago potassium chloride was purchased from one of the most reputable overseas manufacturers. On assay, the contents of one of the drums was identified as ammonium sulphate. This drum had been incorrectly labelled by the manufacturer. Freshly distilled water, a necessary ingredient of all solutions, is subjected to routine electrometrical testing. All raw materials intended for use in intravenous preparations are biologically tested for pyrogens. This is essential as we have repeatedly found that chemicals such as sodium chloride, calcium gluconate, lactic acid, etc., although of analytical reagent grade, were contaminated with pyrogens. The necessity of proper sampling was most emphatically impressed on us when a bag of cane

sugar (used for the manufacture of invert sugar) was recently tested. Although the sample from the top of the bag was pyrogen-free, the bottom sample was heavily contaminated with pyrogen. This bag must have stood on a damp surface at one stage and bacterial growth took place in the moist layers although the physical appearance of the sugar was unchanged.

Question 3. Biological tests of finished products

All finished preparations are assayed chemically and when necessary bacteriologically and biologically. Biological tests are performed on preparations of which the active ingredients cannot be assayed chemically; examples of such preparations are suprarenal cortical extract, pituitary-posterior-lobe extract, etc. Preparations containing antibiotics are assayed microbiologically by methods approved by the Union Health Department. Certain products must be tested by specific methods in order to ensure the absence of harmful substances, e.g. toxin in preparations of toxoid, histamine in liver extract, etc.

Every batch of all injectable preparations is tested bacteriologically for the absence of viable aerobic and anaerobic bacteria and for moulds and fungi. In addition to the routine incubation of the material under test in suitable culture media, a double check is made on several injectable preparations and on all fluid-administration sets by simultaneously sterilizing identical containers filled with culture media heavily inoculated with resistant bacterial spores. The greatest danger to sterility is that of a batch of ampoules or other containers bypassing the autoclave owing to human error. The only safeguard against this very real danger is bacteriological testing of every prepared lot.

Pyrogen tests are performed on every finished batch of injectable preparations which are intended for intravenous use. Pyrogen testing of the bulk solution alone is unsatisfactory. A solution may be pyrogen free in the morning but by the late afternoon bacterial growth might render it pyrogenic. We have found that double-distilled water often becomes pyrogenic if it is allowed to stand overnight. Accordingly, units filled at different times of the day are tested separately.

The question has repeatedly been asked whether a solution which produces pyrogenic reaction in rabbits would do so in humans. We had the opportunity of testing solutions and infusion equipment (their sources of origin were not disclosed) which has caused rigors and high temperature in patients. Rabbits gave, in every instance, unequivocal pyrogenic response. Even a small volume of a solution contaminated with pyrogens can cause severe reactions. We once received ampoules of calcium gluconate for testing which in doses of 5 c.c. caused severe rigor and fever in 2 patients in whom it was injected intravenously. This emphasizes the danger of pyrogen contamination of solutions used for parenteral fluid therapy when 2-5 litres or even more may be infused in 24 hours.

Visual tests. Every single unit from ampoule size to litre bottles is inspected by trained personnel in specially constructed trans-lumination cabinets; all units in which particulate matter is detected is rejected. If the test reveals the presence of pyrogens, the batch is rejected, for the removal of pyrogens is not considered a safe procedure.

Records. Adequate records of every phase of production and of all control tests relating to each batch of solutions manufactured are kept. Before a batch is released the document is scrutinized by a senior member of the staff to verify that all tests have been performed and that the batch conforms with the standards laid down.

The organization and routine performance of all these tests is costly; it requires qualified technical staff, much equipment and, of course, large numbers of laboratory animals.

Licensing of Premises for the Preparation of Intravenous Preparations

Our laboratories are licensed to manufacture therapeutic substances and we have received permission to use the Mark of the South African Bureau of Standards on certain products. Because of this our laboratories are inspected by officials of the South African Bureau of Standards.

Saphar Laboratories Ltd
P.O. Box 643
Johannesburg
24 May 1957

A. Janovics
Medical Director

1. Questions Answered (1957): S. Afr. Med. J., 31, 459.